

introduction to
**ORGANIC
CHEMISTRY**

sixth edition by

A. LOWY

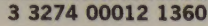
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An Introduction to
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Text-book of Biochemistry

An Introduction to **Organic Chemistry**

By the late ALEXANDER LOWY, Ph.D.
and BENJAMIN HARROW, Ph.D.

SIXTH EDITION

REVISED BY

BENJAMIN HARROW, Ph.D.

Professor of Chemistry

AND

PERCY M. APFELBAUM, Ph.D.

Assistant Professor of Chemistry

Both at The City College

The College of The City of New York

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BENJAMIN HARROW

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SIXTH EDITION

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Dedicated
to the memory of
ALEXANDER LOWY
(1889-1941)

PREFACE TO THE SIXTH EDITION

The cordial reception which the first five editions of the book have received from teachers and students has prompted us to take the opportunity offered by the publishers to prepare a new edition. Besides considerable additional material, the more important recent advances in the field of organic chemistry have been included—at least, such of them as are suitable for an elementary textbook.

Some fifty pages have been added. Emphasis has been placed on modern theories without any desire to overload this phase of the subject.

Among the more specific changes, we may mention a more extended discussion of the electronic concept of valence (throughout the book) and the inclusion of such topics as resonance, substitution in the benzene ring, alicyclic ring structures, and high polymers. The chapter on terpenes has been rewritten, and the list of reference books has been revised and rearranged.

For their kindness in giving permission to reproduce diagrams, the authors wish to thank the following: the Marland Oil Co. (Petroleum Refining); the Foster Wheeler Corporation (Products of Petroleum Refining); The U. S. Industrial Alcohol Co. (Ethyl Alcohol); D. Van Nostrand Co. (two colored charts); and Cain and Thorpe, *Synthetic Dyestuffs and Intermediate Products* (Substituents in Naphthalene Ring).

The authors will at all times welcome suggestions and criticism.

BENJAMIN HARROW
PERCY M. APFELBAUM

PREFACE TO FIRST EDITION

In the preparation of this work the authors have tried to keep a number of objects constantly in mind. In the first place, they desired to embody in the work material which could be satisfactorily treated in a course in which the theory of organic chemistry is covered in two semesters (two hours a week). They were also anxious that such material should include not only the well-recognized basic principles of organic chemistry, but also its more recent and more important applications, the entire story being woven together into a simple and readable narrative.

The authors have also kept in mind the many connecting links that bind organic chemistry to a number of other sciences—to medicine, dentistry, pharmacy; to agriculture; to the biological sciences; hence, the inclusion of such chapters as those dealing with lipoids; nucleoproteins and their decomposition products; plant and animal pigments; enzymes, vitamins and hormones; organic compounds of arsenic and other metals; dyes and stains, etc.

The text can, therefore, be appropriately used in connection with a lecture course, not only by the student who is taking organic chemistry as part of a general academic course, or as preparation for a more extended course in chemistry, but by one who is preparing for the medical, dental, pharmaceutical or other biological sciences.

The book is not intended to act as a guide for laboratory manipulations; details for the preparation of compounds are, therefore, intentionally omitted. Neither, with a few exceptions, are boiling points, melting points or other physical constants included in the body of the work; some of these will be found in the form of a table in the appendix.

To aid the student in naming organic compounds, a brief chapter (XXXVII) is devoted to this topic.

The structure of benzene and its derivatives is shown in heavy and light lines, the heavy lines representing double bonds. This is in accordance with a plan originally proposed by one of the authors.¹

The charts, taken in conjunction with Chapter XXXIV (a brief outline for the identification of organic substances), should serve, to some extent, the purposes of a review.

¹ *Journal of the American Chemical Society*, **41**, 1029 (1919).

A number of charts throughout the text, illustrating the uses of a few important chemicals, have been incorporated if only to give the student some idea of the many and diverse uses to which organic substances may be put.

In the opinion of the authors, the student should at the very outset be given some opportunity for collateral reading; hence, the general references at the end of the book.

The glossary has been added to explain a number of medical terms used in the text.

Photographs of a few of the outstanding leaders in organic chemistry have been included.

The authors have freely consulted various textbooks and journals and they wish to acknowledge their debt to the men responsible for the texts and articles.

For their kindness in giving permission to reproduce diagrams, the authors wish to thank the following: The Marland Oil Co. (Petroleum Refining); R. F. Remler of the Mellon Institute of Industrial Research, and the National Wood Chemical Association (Uses of Methanol, Uses of Acetic Acid, Uses of Acetone, Uses of Formaldehyde); The U. S. Industrial Alcohol Co. (Ethyl Alcohol); D. Van Nostrand Co. (two colored charts); and Cain and Thorpe: "Synthetic Dyestuffs and Intermediate Products" (Substituents in Naphthalene Ring).

The authors are indebted to Dr. Tesh for complete proof-reading and to other members of the Department of Chemistry of the University of Pittsburgh for criticism.

The authors will at all times welcome suggestions and criticism.

ALEXANDER LOWY
BENJAMIN HARROW

NOTE FOR STUDENT

Remember that the laws in chemistry hold for organic as well as for inorganic chemistry. Correlate as many of the new facts with facts with which you are already familiar from your previous studies.

Classification in organic chemistry has been carried to an exceptional degree. One type reaction often gives the key to hundreds of individual reactions. Emphasize, therefore, type formulas and type reactions and make constant use of paper and pencil to practice the writing of formulas and equations.

Periodically refer to the "Replacement of Elements and Groups" on pages 381 and 382.

Chapter XXXVII deals with the nomenclature of organic compounds. It contains a list of the more important organic radicals and ring systems. The student is urged to consult this list from time to time.

L. A. Goldblatt is the editor of a pamphlet, *Readings in Elementary Organic Chemistry* (Appleton-Century, 1938). This book contains original articles on the subject of organic chemistry taken from the literature. Much that is interesting and instructive will be found here. The student is urged to use this volume for his supplementary reading.

Physical constants, such as boiling point, melting point, crystalline form, specific gravity, solubility, refractive index, rotatory power, and color, are in most cases intentionally omitted. The melting and boiling points of a few common compounds are listed on pages 420-423. In general, for information regarding physical constants consult the *International Critical Tables* or handbooks listed under "Reference Books" on page 425.

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CHAPTER I

INTRODUCTION

Long ago man conceived the idea that between the living and the lifeless there is a sharp dividing line. A careful study of the colors of the spectrum, or a consideration of evolutionary problems, might have made him reconsider this view. It would have been more logical to assume that we probably cannot tell just where the "lifeless" ends and the "living" begins. That, indeed, is the modern point of view.

Even as late as a century ago, chemists still had faith in the classification of chemical compounds into "organic" and "inorganic," the organic being distinguished from the inorganic on the supposition that the organic had arisen through some kind of "vital" or "life force," which made it seem quite impossible that a chemist could ever hope to reproduce an organic substance in the laboratory. Formerly, substances of mineral origin were classed as inorganic; those of animal or vegetable origin, as organic.

These notions of organic and inorganic were rudely shaken by the work of *Wöhler*, a distinguished German chemist, who, in 1828, succeeded in preparing urea in his laboratory by heating ammonium cyanate [$\text{KCNO} + (\text{NH}_4)_2\text{SO}_4$]. Now, if any one compound can be called organic, such a distinction certainly belongs to urea, for it is the chief end product of the decomposition of proteins in the body and the principal nitrogenous constituent of the urine.

This epoch-making work of *Wöhler* was not, as is generally supposed, at once accepted unconditionally. Sometimes the scientist does not take to scientific changes any more quickly than the average citizen takes to social or political changes. But in time other examples of the production of organic substances in the chemist's laboratory were recorded, and the old idea became less and less important. Chemists prepared or synthesized acetic acid, fats, alcohol, oxalic acid, mustard oil, oil of bitter almonds, sugars, camphor, uric acid, indigo, adrenaline, protein-like substances, and thousands of others, more or less complex—all, however, typically organic substances. We are still far from having reached the limit. It is conceivable that in the not distant future some of the food we use will be made in the chemist's laboratory. Many are

of the opinion that a judicious combination of the work of the physical chemist and the organic chemist will result, eventually, in solving the riddle of life itself.

We still retain the words "organic" and "inorganic," though we no longer think of them in the time-honored sense. What we call **organic chemistry** may more aptly be called **the chemistry of the carbon compounds**, for that is just what organic chemistry deals with.

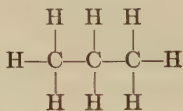
In reality we do not draw the line too sharply. Such compounds as carbon dioxide, carbon monoxide, carbon disulfide, hydrogen cyanide, and the carbonates are usually included in textbooks on inorganic chemistry, though, of course, they are carbon compounds and according to the definition should be included in organic chemistry.

The fundamental laws which the student has taken up in general chemistry apply to organic chemistry with equal or perhaps greater force. If, then, the dividing line between organic and inorganic chemistry is not a sharp one, why the necessity for having these two subdivisions? We shall enumerate a number of reasons.

1. The number of compounds of carbon known today exceeds 250,000, and the number of compounds that do not contain carbon is only about 27,000.

2. In general, organic and inorganic compounds show marked differences in solubility, the organic compounds being usually soluble in ether, alcohol, chloroform, benzene, etc., whereas the inorganic are not; many of the inorganic compounds are soluble in water and the organic ones are not.

3. The atoms of carbon have the unique property of combining with one another to form chain-like structures—a property not frequently shown by other elements: for example,



4. Organic compounds are, as a rule, less stable than inorganic; they are much more easily susceptible of chemical and physical changes. Organic compounds are decomposed at relatively low temperatures.

5. "Type" reactions are quite frequent in organic chemistry. For example, there are hundreds of organic compounds that react with nitric acid to form "nitro" compounds, which, in turn, react with reducing agents to yield "amino" compounds, etc.

6. There is often a marked difference in the velocity of reaction. The change from one organic compound to another is usually a relatively slow

process, whereas the transformation of inorganic substances is often practically instantaneous.

7. Reactions in organic chemistry are, as a rule, mostly non-ionic, the solutions being non-conductors of electricity, whereas reactions in inorganic chemistry are largely ionic. This explains, for example, why, when solutions of sodium chloride and silver nitrate are mixed, an immediate precipitate of silver chloride is obtained, whereas we get no precipitate upon mixing solutions of pure carbon tetrachloride (CCl_4) and silver nitrate. Many types of organic acids and salts ionize.

8. Reactions in organic chemistry often tend to become quite complex, and there are possibilities of many "side" or "secondary" reactions.

9. The complexity in structure exhibited by some organic compounds is quite unknown among inorganic compounds.

10. Organic compounds often show a property called **isomerism**, which we shall discuss later in some detail (p. 20), but this phenomenon is very little known in inorganic chemistry. For example, when we write HNO_3 we have reference to nitric acid, and to nitric acid alone, but when we write $\text{C}_2\text{H}_6\text{O}$ we may mean either ethyl alcohol or methyl ether, and the only way we can distinguish the one from the other is by writing graphic or structural formulas, which give some idea of the arrangement of the atoms within the molecule. That is the reason why graphic or structural formulas are used so extensively in organic chemistry (pp. 9, 14).

Importance and Applications. We have already mentioned the fact that more than 250,000 compounds are grouped under organic substances. Many of them find various applications in our daily life. Some are so common that merely mentioning their names will suggest to the student many of their applications. Picking a few of these substances more or less at random, we may refer to starch, sugar, fats, oils, proteins, paper, rayon, soap, explosives, photographic developers, Bakelite, anesthetics, disinfectants, antiseptics, dyes, drugs, waxes, ether, natural gas, perfumes, glue, citric acid, alcohol, saccharin, artificial food colors, caffeine, cellulose, camphor, rubber, flavoring essences, gasoline, Vaseline, coal tar, glycerin, aniline, indigo, salvarsan, and lacquers (Duco, etc.). It may be added that the various transformations which the foodstuffs and cellular tissue undergo in the plant and animal kingdom, involving complex syntheses and decompositions, are essentially those which can best be studied by the organic chemist.

Within the last few years there has been an extraordinary expansion in the chemical industries involving uses of various chemicals. A few of the newer products may be mentioned: Nylon and Vinyon and other synthetic fibers; wetting agents; synthetic plastics and resins; chlorinated

phenols for use as antiseptics and preservatives; lubricating oils; synthetic rubbers exhibiting physical and chemical properties superior to those of rubber; nitrated aliphatic hydrocarbons; and high-octane gasoline from the catalytic conversion of hydrocarbons.

Many types of organic chemicals are now obtained from acetylene, ethylene, butane, pentane, etc., for example, alcohols, ethers, aldehydes, acids, and amines.

Other Sciences Based on Organic Chemistry. Physiological (or bio-) chemistry (which deals with the chemical processes that take place in animals and plants), food chemistry, and organic analysis all have their basis in organic chemistry. Various aspects of medicine, dentistry, and pharmacy require training in organic chemistry. We shall illustrate this interdependence with one or two examples.

The structural formulas for cholesterol and ergosterol have now been related to the formulas deduced for the sex hormones. Some of the more powerful synthetic cancer-producing substances belong to compounds similar in structure.

In the field of vitamins the organic chemist has worked out the structures of most vitamins, including vitamin K. Furthermore, the structures of some of the vitamins are related to those of certain oxidizing enzymes of the body. For example, the vitamin nicotinic acid is related to an enzyme which takes part in biological oxidations. This may explain the need for certain vitamins.

Thanks to the organic chemist, the synthesis of glutathione, an important constituent of cells, is now an accomplished fact. Beginning with benzyl alcohol the chemist has developed a new and elegant method for synthesizing polypeptides.

Heavy hydrogen (deuterium) and several isotopes of nitrogen, phosphorus, etc., are now being successfully used to follow the chemical changes in the body. A number of enzymes have been shown to be proteins, and others resemble the hemoglobin type of pigments. Recent study by the chemist has yielded information concerning the protein nature of viruses. Nor can one overlook the sensational discoveries of "sulfa" drugs and penicillin.

Sources and Occurrence of Organic Compounds. A. Organic compounds may be traced to either the plant or animal kingdom. Out of carbon dioxide, water, and various constituents from the soil, in the presence of light, the plant builds a veritable galaxy of substances: sugars, starches, cellulose, alkaloids (morphine in opium, nicotine in tobacco), acids (citric and tartaric), salts ("tartar" in grapes), esters (flavoring substances of fruits), essential oils (peppermint, lemon), camphor, vegetable oils (linseed, cottonseed, olive), herbs (from which drugs

are made and which were so largely used in days gone by), gum arabic, flavoring substances (vanilla), dyes (indigo, logwood, fustic), perfumes, tannin (from nutgalls), etc.

B. Plants and animals furnish us with fats, proteins, carbohydrates, enzymes, and vitamins, and we often go to the animal kingdom for a number of other products, such as urea, uric acid, gelatin, toxins, and antitoxins.

C. Destructive Distillation of Coal. Soft coal, when strongly heated in a retort, breaks down into a number of (chemically) simpler substances. The conversion of a complex substance into a number of simpler substances by the aid of heat (in the absence of air) is known as "destructive distillation." The destructive distillation of coal yields coal gas (illuminating gas), ammonia, coke, and coal tar. Coal tar, at one time discarded as a useless by-product, is now the starting point for any number of organic products (some 225 compounds have so far been isolated). Out of coal tar we get benzene, toluene, naphthalene, anthracene, carbolic acid, the cresols, etc.; and these substances (the source of many aromatic compounds) in turn yield thousands of other organic compounds, many of them of great value as dyes, perfumes, drugs, etc. (see chart facing p. 236). *Perkin*, an Englishman, was the first (in 1856) to prepare a coal-tar dye, but the development of the dye industry is due largely to the Germans, who, prior to World War I, were responsible for much research work in this field. Later developments ensured the establishment of permanent dye and related industries in the United States and elsewhere.

D. Destructive Distillation of Wood. The important products obtained from wood are acetic acid, methanol (wood alcohol), acetone (indirectly), wood tar, combustible gases, and charcoal. Many of these products are now synthesized in large part, and the wood distillation industry is of less importance.

E. Acetylene. This is derived from such natural sources as limestone, coal, and water. A large number of important organic compounds are obtained from acetylene. (Chart facing p. 94.)

F. Fractional Distillation of Petroleum. In a mixture of two or more liquids having different boiling points, the liquids may usually be separated from one another by a process of distillation, the liquid with the lowest boiling point distilling over first. The process which separates two or more liquids by making use of their different boiling points is called fractional distillation. The fractional distillation of petroleum yields a number of important commercial products, such as naphtha, gasoline, kerosene, gas oil, lubricating oil, cylinder oil, and Vaseline.

G. Natural Gas. Within the past few years there have been important new developments due to the production of compounds of practical

importance from natural gas. Many of these new compounds have been synthesized from ethylene as the starting material. (Chart facing p. 80.)

H. Fermentation. For a long time it was supposed that, in the conversion of sugar into alcohol by means of yeast, the living cells of the yeast were primarily responsible for the change. We now know that what brings about this change is not the cells themselves, but substances produced by the cells, known as enzymes. Changes analogous to the conversion of sugar into alcohol are known as fermentation. The sweet apple juice turns to cider (owing to the formation of alcohol), and finally to cider vinegar (owing to the oxidation of the alcohol into acetic acid). Milk on standing, or when "inoculated" with bacteria, becomes sour, owing to the conversion of lactose (milk sugar) into lactic acid.

I. Putrefaction. Putrefaction may be defined as the decomposition of animal or vegetable substances brought about largely by microorganisms, resulting in diverse products, some of which have a foul odor. Among the products of putrefaction are amines, fatty acids, ammonia and its compounds, hydrogen sulfide, and methane.

Purification of Organic Compounds. Before its physical constants and chemical analyses (qualitative and quantitative) can be obtained, a compound must be prepared in a pure state. For details of the methods of preparing chemically pure substances, we must refer the student to appropriate laboratory textbooks (see p. 426), and only the barest outline will be given here.

A compound as first prepared is generally in an impure state. It may be purified by one or more of several processes, such as crystallization, distillation, sublimation, extraction, dialysis, precipitation, or decolorization (for details refer to laboratory manuals, p. 426). Almost all pure organic compounds have a definite melting point (m.p.), or boiling point (b.p.), or both. The melting or boiling point of the compound is, therefore, determined after the preliminary process of purification. A definite melting or boiling point is an important criterion of purity; in addition, the specific gravity, solubility, crystalline structure, refractive index, optical activity, etc., are also used. The principles involved, as well as the details of manipulation, will become familiar to the student as a result of his laboratory work. The pure product having been obtained, the next step is an analysis of it.

Elements Present in Organic Compounds. Numerous as the compounds of carbon are, most of them contain but two to five different elements. There are hundreds of compounds which contain merely the elements carbon and hydrogen. These are known as hydrocarbons. Methane (CH_4), benzene (C_6H_6), naphthalene (C_{10}H_8), and anthracene

($C_{14}H_{10}$) are examples. Many contain the element oxygen in addition to carbon and hydrogen: for example, the sugars, fats, starches, alcohols, ethers, acetic acid, and glycerol. Many are composed of carbon, hydrogen, and nitrogen, as hydrocyanic acid and aniline. Examples of compounds containing carbon, hydrogen, oxygen, and nitrogen are some of the alkaloids, proteins, indigo, and urea; and among those containing carbon, hydrogen, and a halogen are carbon tetrachloride and iodoform.

Often, in addition to the elements already mentioned, we find sulfur and phosphorus. Many of the proteins contain appreciable quantities of sulfur, and the phosphatides, such as lecithin and cephalin, which are important cellular constituents, contain phosphorus. Among the better-known sulfur-containing organic compounds are the "sulfa" drugs.

Elements other than those already mentioned are often found. Since the pioneer work of *Ehrlich* on salvarsan, very many organic compounds of arsenic, antimony, bismuth, and mercury have been prepared. An organic compound of lead, lead tetraethyl, is used to prevent "knocking" in automobile engines (p. 218). Many salts of organic acids, such as sodium, potassium, calcium salts, etc., are found in nature or may be prepared in the laboratory.

Analysis of Organic Compounds. Detailed directions are given in laboratory manuals. Before a quantitative analysis of a compound is made, a qualitative analysis, involving the detection of the elements present, is undertaken. In the course of the qualitative analysis, carbon in most organic compounds may be detected by heating the compound with copper oxide, the carbon thereby being oxidized to carbon dioxide, the presence of which may be shown with lime water. The same process oxidizes any hydrogen present to water, which is usually seen to collect in the upper (cooler) part of the tube. Nitrogen may be detected either by heating the substance with soda lime ($NaOH + CaO$), thereby converting the nitrogen into ammonia, or by fusion with metallic sodium, whereby sodium cyanide is formed ($Na + C$ of organic compound $+ N$), which is then converted into ferrocyanide by treating with a ferrous salt, and ultimately to "prussian blue" on acidification. Halogens may be recognized by heating the compound with copper oxide in a non-luminous flame, whereby a green coloration is obtained, due to the volatilization of the copper halide, or by making use of the sodium fusion test, whereby the halogen is converted into the corresponding sodium salt, which may then be tested with silver nitrate. The halogen in organic combinations is mainly in a non-ionizable form, and therefore does not react with a solution of silver nitrate prior to its decomposition.

If sulfur is present it may be recognized by fusion with sodium, whereby sodium sulfide is formed. In water solution sodium sulfide

forms a black precipitate of lead sulfide with lead acetate solution. The sulfide ion also gives a reddish purple color with sodium nitroprusside solution.

Phosphorus and any of the other elements (such as the metals) are detected just as in inorganic analysis. The test for phosphorus requires a preliminary fusion with an oxidizing mixture (such as potassium nitrate and sodium carbonate).

In many organic compounds oxygen can be detected by vaporizing the compound and passing the vapors over glowing charcoal, then through barium hydroxide solution. If oxygen is present in the compound, it will be converted to carbon dioxide and precipitated as barium carbonate.

Many of the qualitative tests serve as the basis for the quantitative determinations. The carbon dioxide and water formed by the oxidation of a compound containing carbon and hydrogen are collected and weighed, and, from the amounts of the products formed, the percentages of carbon and hydrogen in the original compound are calculated. The nitrogen in a compound may be determined either by the Kjeldahl method, whereby the element is converted into ammonia, or by the Dumas absolute method, whereby nitrogen gas is set free and its volume measured.

In the determination of the halogens, the compound is either oxidized with fuming nitric acid in the presence of silver nitrate, the resulting silver halide weighed, and the halogen calculated; or the compound is heated with pure calcium oxide, and the halogen in the resulting calcium halide is determined either by precipitation or titration with silver nitrate.

Sulfur in an organic compound is determined by oxidizing it with fuming nitric acid to sulfuric acid. It is then precipitated as barium sulfate with barium chloride. The percentage of sulfur is calculated from the weight of barium sulfate.

For estimating phosphorus and other elements, the methods outlined in inorganic quantitative analysis are followed.

No simple method is available for oxygen in an organic compound. The general procedure is to determine the percentage of all the other elements present in the compound, subtract the total from 100, and "call" the difference the percentage of oxygen.

The principles underlying the analytical methods are quite simple, but the details for the quantitative determination of C, H, N, and the other elements are rather complex.

Practically all quantitative organic analyses are now carried out by micro methods which require much less material (a few milligrams) and less time than the older macro methods. As a matter of fact, micro

methods have lately been applied to many other types of laboratory procedure, analytical and synthetic.

The analysis just discussed is what is known as "ultimate" or "elementary" analysis. It refers to the percentages of the elements present in the compound. There is another type of analysis, known as "proximate," with which the clinical, pharmaceutical, or food chemist is generally concerned. Proximate organic analysis deals with the determination of ingredients present in a mixture, such as the fat or protein in milk, or the various nitrogenous constituents and sugar in urine, or the percentage of alcohol in wine, etc.

Quantitative analysis enables us to arrive at what is known as the "empirical" or simplest formula; but this may not necessarily prove to be the true or "molecular" formula. For example, a quantitative analysis of acetylene and benzene would yield the same empirical formula for both, namely, CH ; yet acetylene is written C_2H_2 and benzene C_6H_6 . In order to arrive at the actual or molecular formula, whether C_2H_2 or C_6H_6 , we must further proceed to a molecular-weight determination, based on vapor density, or boiling point, or freezing point, etc. Here again the reader is referred to laboratory manuals of physical chemistry for further details.

The Fundamental Bases Underlying the Structural Theory of Organic Chemistry. As we have seen (p. 9), the existence of isomerism makes necessary the writing of graphic or structural formulas which not only give the ratio of the various atoms in the molecule (empirical formula), or even the actual numbers of these atoms (molecular formula), but also attempt to show the relative atomic arrangement within the molecule.

Structural formulas thus are fairly precise symbols of the compounds they represent and must, as far as possible, agree with the structural formulas of the substances which were used to make the compound in question, and also with the formulas of compounds obtained by further treatment. The writing of such structures has become an integral part of theoretical organic chemistry and is based on certain concepts first enunciated by *Kekulé*, *Le Bel*, *van't Hoff*, etc.

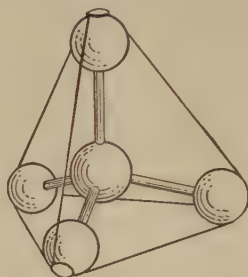
1. The valence of carbon, almost without exception, is four,¹ and it is represented ² as



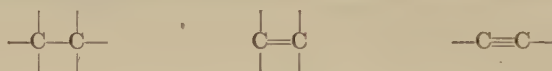
¹ There seem to be several striking exceptions, such as CO , $\text{C}=\text{NOH}$, $\text{R}-\text{N}=\text{C}$, and $(\text{C}_6\text{H}_5)_3\text{C}$. From the electronic point of view, however, these structures are not exceptional but involve different arrangements of electrons.

² It is suggested that at this point the instructor illustrate by means of models the probable spatial arrangement (in the form of a regular tetrahedron) of the methane molecule.

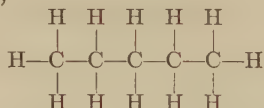
where any one bond bears exactly the same relationship to the carbon atom as any other bond. These valences may be represented as directed toward the corners of a regular tetrahedron, constructed around the carbon atom as a center, and they are, therefore, equidistant from each other in space.



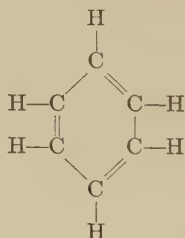
2. Carbon atoms may be united by single, double, or triple bonds:



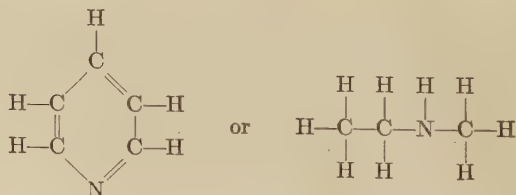
3. Carbon atoms may form a "straight" or "open" chain in "aliphatic" compounds; for example,



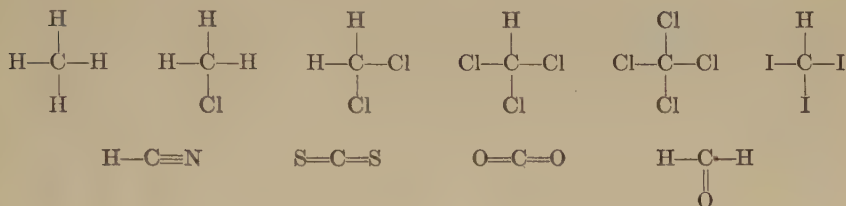
4. Carbon atoms may form a "closed" chain or ring in "cyclic" compounds; for example,



5. Other elements besides carbon may enter a carbon chain or ring; e.g.,



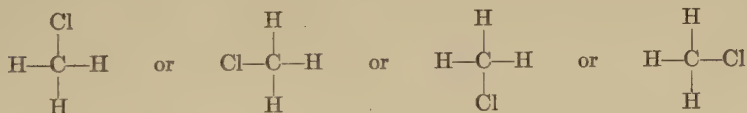
6. Elements may substitute for one another in compounds; that is, one element in a compound may be removed, and another may take its place: for example,



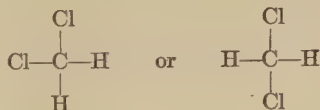
It must not be supposed that, when we write methane, $\text{H}-\text{C}-\text{H}$, we

have any intention of fixing the atoms in space. In any case—and this has already been referred to—two-dimensional configurations cannot truly represent the structure of any form of matter. The structural formula is a conventional two-dimensional projection of the tetrahedral spatial formula. On the basis of these two-dimensional formulas we can explain, and even predict, the behavior of organic compounds.

We do wish to emphasize that in the formula for methane the four hydrogen atoms are to be regarded as of equal value, so that, when a hydrogen atom is replaced by a chlorine atom, it does not matter whether we write



for they all represent one and the same compound, namely, monochloromethane; nor, if two hydrogen atoms are replaced by two chlorine atoms, does it matter whether we write



for both represent the same compound, dichloromethane.

These relationships, and some others, are summed up in the concept of the tetrahedral carbon atom and are shown clearly in actual models. Physical measurements have confirmed the chemist's idea that the four

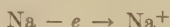
valences of carbon are directed outward toward the corners of a tetrahedron imagined circumscribed about the atom. Two carbons united by a single bond are represented by two tetrahedra fastened together through one corner of each. When the atoms are united by a double bond the tetrahedra must be attached at two pairs of corners—that is, along an edge of each.

Physical measurements (*electron diffraction*) also show that atoms act as though each had a fixed radius for any given type of bond. For any given types of bonds, moreover, the angles between the bonds are practically constant from compound to compound, and they can be calculated from the tetrahedral picture. It is therefore possible to construct blocks of such sizes and shapes that models can be made from them which give a rather accurate representation of the actual geometrical relationships of atoms in molecules.¹ It should also be remembered in this connection that in actual molecules the atoms are not at rest with respect to one another but are always undergoing vibrations of small amplitude.

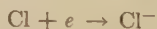
Electron Conception of Valence. For practical purposes, the chemist has found the *Lewis-Langmuir* concept of the electronic structure of the atom very fruitful. We shall encounter several examples of its usefulness throughout succeeding chapters.

It may be well now to review our fundamental ideas of atomic linkage and to consider how they apply to carbon compounds.

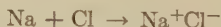
In many simple inorganic reactions, when one element combines with another, there is actually a transfer of one or more electrons; for example, in the combination of sodium and chlorine,



and



so that



This is, of course, the ionic linkage of electrolytes, and we remember that polarities are assigned to the ions on the basis of their behavior on electrolysis and on double decomposition; for example, metallic ions are cations and therefore positive; furthermore, other ions which replace them in double decompositions are assigned the same polarity. A transfer of electrons of this type is known as *electrovalence*, resulting in a *polar* (heteropolar) linkage between the atoms concerned.

In many cases we find a *sharing* of electrons within a compound

¹ See, for example, the Fisher-Hirschfelder Atom Model Set, supplied by the Fisher Scientific Co., Pittsburgh, Pa.

(*covalence*). For example, hydrogen, ethylene, and water may be represented as

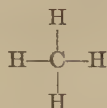


In organic chemistry the covalent or *non-polar* (homopolar) bond is much the more common.

Carbon has a valence of four. It has four electrons in its outer shell. It does not, as a rule, form negative or positive ions. We say, therefore, that, when carbon combines with another element to form a compound, there is a *sharing* rather than a *transfer* of electrons. On this basis, methane is represented as

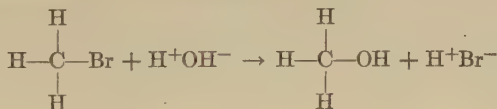


When we compare this electronic formulation with the classical method of writing the structural formula for methane,

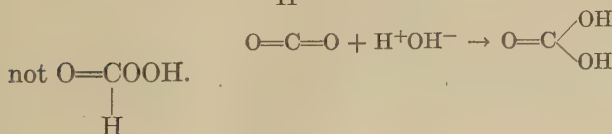


we see that each covalent bond is the equivalent of two shared electrons. *G. N. Lewis* was the first to advance the hypothesis that the two electrons shared by the two atoms constitute the chemical bond.

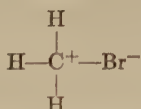
The two extremes in chemical bonding are represented by covalence and electrovalence. Many compounds, however, manifest a behavior intermediate between that of the polar electrolytes and that of the absolutely non-polar substances. Even though most organic compounds are written as covalent structures, and are non-ionic, they show definite evidences of polarity in many reactions. For instance,



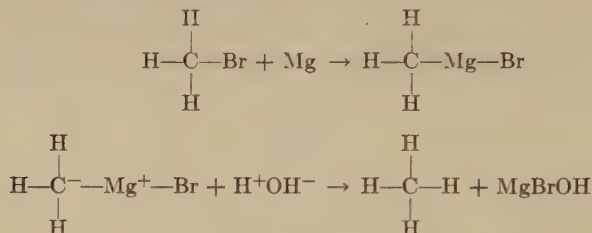
but we do not get $\begin{array}{c} \text{H} \\ | \\ \text{H}-\text{C}-\text{H} \\ | \\ \text{H} \end{array} + \text{HOBr}$. Or



It is therefore reasonable to assume that, in the original carbon compound, we have, at least at the moment of reaction, a definite polarity:

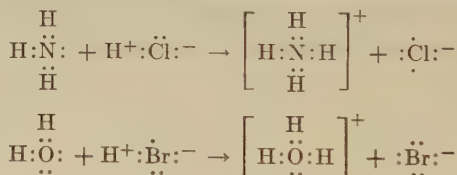


It is interesting to note, too, that the polarity of the same group can be changed by a simple transformation:



Inorganic molecules (H_2O , NH_3 , etc.) also show this dipolar behavior, which, in many cases, can be detected by physical means (*dipole moment*).

On the basis of modern theory, a third type of linkage is used to represent another mode of combination, such as occurs in the formation of ammonium compounds and in the dissociation of acids in water:

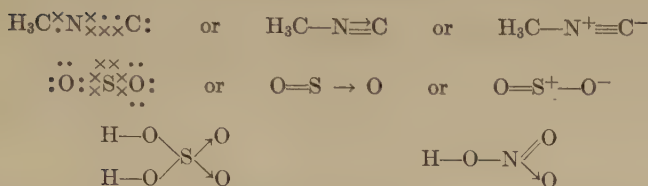


The proton of the acid shares with nitrogen or oxygen a pair of electrons which either of these elements (the *donor*) can share with an atom like hydrogen (the *acceptor*). This displacement of electrons constitutes a *coordinate covalence* (dative covalency), the linkage being known as a *semipolar bond*.

With elements other than hydrogen, also, a similar linkage serves to explain, on the basis of the *Lewis* concept, the stability of compounds by means of simple structural formulas:

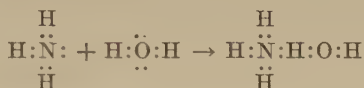


¹ The dots and the crosses represent electrons derived from different elements. In this example, the dots represent electrons derived from the carbon atom, and the crosses represent electrons derived from the oxygen atom.



Semipolar bonds can be differentiated from covalent bonds by physical measurements (*parachor*).

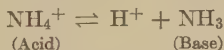
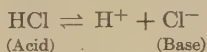
In the case of some hydrogen compounds, a similar linkage is used to interpret certain unusual phenomena, such as the fact that ammonium hydroxide, formed from NH_3 and H_2O , is a weak base, that is, dissociates but slightly:



A so-called *hydrogen bond* forms a temporary linkage between H and O. The same sort of bond is used to explain the existence of hydrogen fluoride as H_2F_2 instead of HF.

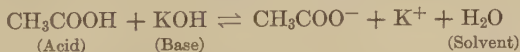


In connection with this subject, we might point out that the modern generalized definition of acids and bases (Brönsted, Lowry) has been found very useful in organic chemistry.

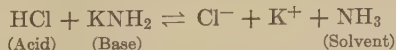


Acids are substances which evolve protons; bases combine with protons. Conjugate acid and base are a pair defined by each of the equations above.

In water solution ($2\text{H}_2\text{O} \rightleftharpoons \text{H}_3\text{O}^+ + \text{OH}^-$),



In liquid ammonia solution ($2\text{NH}_3 \rightleftharpoons \text{NH}_4^+ + \text{NH}_2^-$),



As we proceed, we shall note applications of these useful concepts to organic compounds and their reactions.

Classification of Organic Compounds. There are three main divisions: the **aliphatic**, the **aromatic**, and the **heterocyclic** compounds.

The aliphatic compounds are related to methane, CH_4 , and are "open chain." They get their name from the fact that animal and vegetable fats belong to this series.

The aromatic ("ring" or "cyclic") compounds are related to benzene, C_6H_6 , and many are characterized by fragrant odors; hence the name.

The line of demarcation between aliphatic and aromatic compounds is not a sharp one, for not all aliphatic compounds can be directly traced to fatty substances, nor do all aromatic compounds have odors. On the other hand, many aliphatic compounds possess very characteristic odors. Nevertheless, there are, as a rule, some general differences which help to differentiate these two divisions, perhaps the most important being differences in a number of chemical properties.

Ring structures containing carbon and other elements are designated as heterocyclic compounds.

It is of interest, in noting the industrial developments of organic chemicals, that the emphasis, at first, was on the development of compounds belonging to the aromatic series. More recently, and particularly in the United States, the possibilities of products belonging to the aliphatic series have been much exploited. (See charts facing pp. 80 and 94.)

CHAPTER II

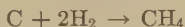
SATURATED HYDROCARBONS OR PARAFFINS. PETROLEUM

As its name implies, a hydrocarbon is a compound containing hydrogen and carbon.

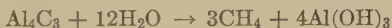
Methane, CH_4 , is the simplest compound of the hydrocarbon group.

Occurrence. The decomposition of vegetable and animal matter gives rise to this gas. One of the gases arising from marshes is methane, hence its name, "marsh gas." It is also one of the gases produced in intestinal putrefaction. It is an important component of natural gas (80 per cent and above) and coal gas (30–40 per cent). Fires and explosions in coal mines are mainly due to the ignition of mixtures of methane and air; hence methane is also known as "firedamp."

Preparation. Methane may be synthesized from its elements by passing hydrogen over carbon in presence of nickel (catalyst) at 475° .



It may also be obtained by the action of water on certain carbides, such as aluminum carbide:



This reaction is of interest since it led Moissan, the French chemist, to speculate on the origin of natural gas and petroleum. He held the origin of natural gas to be the action of water on various metallic carbides. It must be remembered that methane is not always formed when water acts on a carbide; the student will recall, for example, that water reacts with calcium carbide to yield acetylene.

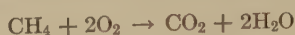
The usual laboratory method for producing methane depends upon heating a mixture of anhydrous sodium acetate and soda lime ($\text{NaOH} + \text{CaO}$):



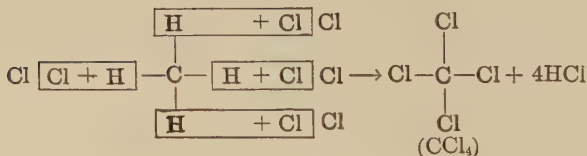
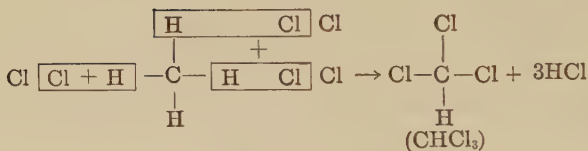
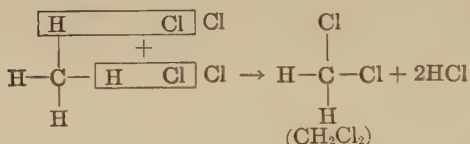
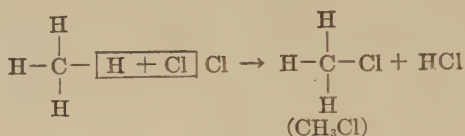
Sodium acetate is the sodium salt of acetic acid, $\text{CH}_3 \cdot \text{COOH}$. Acetic acid, in turn, may be regarded as methane, CH_4 , having one of its hydrogens replaced by the COOH group, known as the "carboxyl" group.

18 SATURATED HYDROCARBONS OR PARAFFINS. PETROLEUM

Properties. Methane has high fuel value. It is a colorless gas with a slight odor, and it burns with an almost non-luminous flame:



The chemical properties of methane are those of the saturated hydrocarbons, of which methane is the first member. Methane is an inactive and stable compound. Methane and other hydrocarbons of this series are known as **paraffins**, which means "little affinity." The common reagents, such as hydrochloric, nitric (under the usual conditions), sulfuric, and chromic acids, and sodium and potassium hydroxides, do not react with it. On the other hand, the halogens, such as chlorine and bromine, react rather vigorously with methane, particularly in the presence of sunlight:



You will notice, in these examples, that the chlorine replaces the hydrogen in the molecule. Whenever an element or a group of elements replaces hydrogen in an organic compound, the process is known as "substitution." Such reactions are characteristic of saturated hydrocarbons. CH_3Cl , CH_2Cl_2 , CHCl_3 , and CCl_4 are chlorine substitution products of methane.

CH_3Cl = methyl chloride or monochloromethane;
(CH_3 = methyl group) (monovalent).

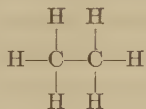
CH_2Cl_2 = methylene chloride or dichloromethane;
(CH_2 = methylene group) (divalent).

CHCl_3 = trichloromethane or chloroform.

CCl_4 = tetrachloromethane or carbon tetrachloride.

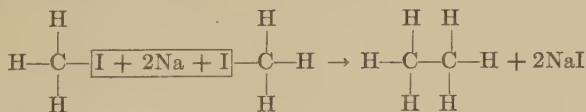
Many of these names need not be memorized. If the student will but remember that these compounds are substitution products of methane, he will have little difficulty in naming them. In CH_3Cl , for example, the compound may logically be regarded as methane in which one of the hydrogen atoms has been replaced by chlorine; hence the name "monochloromethane." But it must also be remembered that the CH_3 group is known as a "methyl" group; hence also the name "methyl chloride."

Ethane, C_2H_6 . This is the second member of the paraffin series, and in its general physical and chemical properties it shows resemblances to methane. It is found in natural gas and petroleum and is separated from other hydrocarbons by fractional distillation. It finds use as a fuel in lighter-than-air craft and as a refrigerant, being readily liquefied under pressure. Its formula is represented by



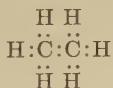
and it differs from methane by CH_2 . It may be regarded as methane in which one of the hydrogens is replaced by a CH_3 group; that is, $\text{CH}_3 \cdot \text{CH}_3$, methylmethane, or dimethyl.

Further light on the structure of ethane is shed by the way in which it can be synthesized. Methyl iodide reacts with sodium in the following way (*Wurtz synthesis*):

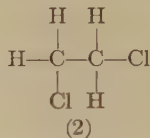
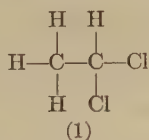


In other words, the formation of ethane is here shown to be a coupling of two methyl groups.

The electron structure for ethane can be represented as

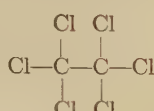
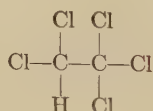
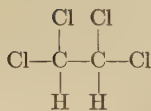
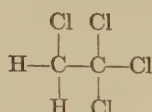
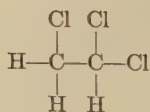
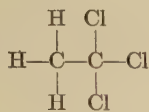


Isomerism. Experience has shown that only one monosubstitution product of ethane can be obtained, but it is possible to obtain two disubstitution products, both having the same molecular formula, $C_2H_4Cl_2$, but differing in physical and chemical properties. Here we have clearly a case of isomerism, and the graphic formulas bear this out:



for in (1) we see two chlorine atoms attached to the same carbon atom, and in (2) the two chlorine atoms are attached to two different carbon atoms. Whenever we have two or more compounds having the same molecular formula, but differing in physical and chemical properties, we have an example of isomerism, and the individual compounds are known as isomers. Let us illustrate isomerism with an analogy. Suppose we take the figures 4, 7, 5. It obviously makes very much difference whether we write 475 or 754 or 547 or 745 or 574 or 457. Yet all we have done is to *rearrange* the figures; and by merely rearranging the numerals we have obtained *totally different* numbers. So it may be with two compounds such as are illustrated above: they may have the same molecular formulas, yet be quite different substances because of the different *arrangement* of the atoms within the molecule.

Experience has also shown that there are but two tri-, two tetra-, one penta-, and one hexa- substitution products of ethane; and the student can confirm this by studying the graphic formulas:



In naming substitution products of ethane, the system adopted for methane is used:

CH_4
Methane

CH_3
Methyl radical

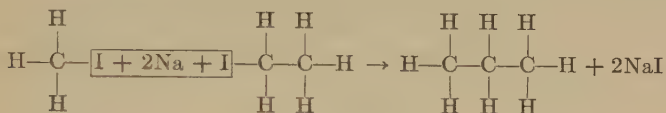
C_2H_6
Ethane

C_2H_5
Ethyl radical

C_2H_5I , for example, is ethyl iodide, or iodoethane, and C_2H_5OH is ethyl alcohol, or hydroxyethane.

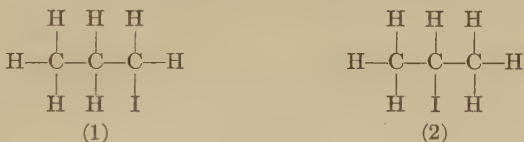
The name for the radical corresponding to the hydrocarbon is obtained by changing the suffix *-ane* into *-yl*.

Propane, C_3H_8 . We have seen that ethane, C_2H_6 , may be regarded as methane, CH_4 , to which CH_2 has been added. Similarly, propane, C_3H_8 , may be regarded as ethane, C_2H_6 , to which CH_2 has been added, or as C_2H_6 in which one of the hydrogens has been replaced by a CH_3 group. Its structure becomes evident by examining its synthetic method of preparation. Ethyl iodide and methyl iodide react with sodium to form propane. The Wurtz reaction was also used in the synthesis of ethane and may be utilized in the synthesis of other hydrocarbons.



In this reaction ethane and butane, C_4H_{10} , are also produced.

We pointed out that in ethane we have but one monosubstitution product and two disubstitution products, and we saw how the structural formulas helped to explain these facts. When we come to propane, we find that two monosubstitution products are possible, one differing from the other in physical and chemical properties. Here again the structural formulas are helpful in explaining experimental facts,



for it will be seen that in (1) the iodine atom is attached to a carbon atom which in turn is attached to two hydrogen and one carbon atoms, whereas in (2) the iodine atom is attached to a carbon atom which in turn is attached to two carbon and one hydrogen atoms.

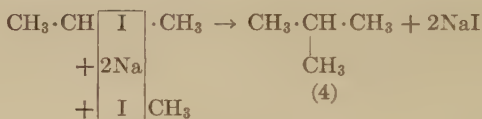
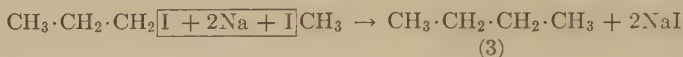
Propane is used as a fuel and refrigerant, and liquid propane is used for refining lubricating oil. "Pyrofax" gas, a fuel sold in various parts of the country, is essentially propane.

Butanes, C_4H_{10} . Two compounds with this formula are known. In the preceding paragraph we pointed out that there are two isomeric

propyl iodides, which, for convenience, we shall now write according to the "structural" or "constitutional" formulas.

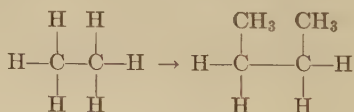


Now, it may be asked, what will happen if first (1) and then (2) are treated with methyl iodide in the presence of sodium? Are we going to get two identical compounds? This is hardly likely, since (1) and (2) are different. In reality, the two compounds obtained are different—different in properties, but alike in having the same molecular formula, C_4H_{10} .



(3) and (4) are isomeric, (3) being known as normal ("straight-chain") or *n*-butane, and (4) as *iso*- ("branched-chain") butane.

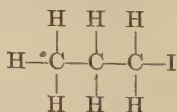
If two of the hydrogens in ethane which are attached to two different carbon atoms are replaced by methyl groups, we get butane or symmetrical dimethylethane:



If, however, the two hydrogen atoms replaced by two methyl groups are on the same carbon atom, then we get isobutane, or unsymmetrical dimethylethane.

The butanes are used for refrigerating purposes and as low-boiling extraction solvents.

¹ Periods are often used in place of bonds when writing structural or constitutional formulas, so that $\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_2\text{I}$ really means $\text{CH}_3-\text{CH}_2-\text{CH}_2\text{I}$, which in turn indicates



As the student proceeds with his studies in organic chemistry, he will find it unnecessary to indicate either dots or dashes for at least some of the simpler types of compounds.

Hydrocarbon	Corresponding Radicals	Names for Radicals
$\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_3$	$\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_2 -$ $\begin{array}{c} \text{CH}_3 \\ \diagup \\ \text{CH} - \\ \diagdown \\ \text{CH}_3 \end{array}$	Propyl Isopropyl
$\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_3$	$\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 -$ $\begin{array}{c} \text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH} - \\ \\ \text{CH}_3 \end{array}$	<i>n</i> -Butyl Secondary (<i>sec</i> -) butyl
$\text{CH}_3 \cdot \text{CH} \cdot \text{CH}_3$ CH_3	$\begin{array}{c} \text{CH}_3 \cdot \text{CH} \cdot \text{CH}_2 - \\ \\ \text{CH}_3 \end{array}$ $\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3 - \text{C} - \\ \\ \text{CH}_3 \end{array}$	Isobutyl Tertiary (<i>tert</i> -) butyl

(Note: *Iso*- as a prefix refers to compounds containing $\begin{array}{c} \text{CH}_3 \\ \diagup \\ \text{CH} - \\ \diagdown \\ \text{CH}_3 \end{array}$ connected to a normal chain.)

Pentanes, C_5H_{12} . Three pentanes are known:

$\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_3$ *n*-pentane

$\text{CH}_3 - \text{CH} - \text{CH}_2 \cdot \text{CH}_3$ isopentane

CH_3

CH_3

$\text{H}_3\text{C} - \text{C} - \text{CH}_3$

CH_3

tetramethylmethane or neopentane

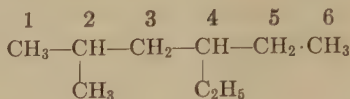
(A "neo" hydrocarbon has four groups attached to one carbon atom.)

As we go up in the paraffin series, the number of isomers becomes increasingly greater.

Nomenclature of Saturated Hydrocarbons. It can be seen that the names given so far offer very few clues to the structures of the compounds they designate. As we proceed further in the group, this traditional nomenclature makes for great confusion, since more modifications are necessary to distinguish between increasing numbers of isomers. The system of the International Union of Chemistry, the so-called Geneva system, provides for simple names, each of which describes a compound and distinguishes it from all others. For saturated hydrocarbons, the Geneva names are made up as follows:

Select the longest straight (continuous) chain of carbon atoms in the molecule and number the carbon atoms consecutively from one end;

select that end which would lead to the use of the smallest numbers to locate the substituents. Consider the side chains as substituents. For example,



is named 2-methyl-4-ethylhexane (and not 3-ethyl-5-methylhexane).

The table on p. 25 includes a few *normal* hydrocarbons and the corresponding monovalent radicals.

From the table we conclude the following:

1. Every hydrocarbon in this series is saturated (single bonds).
2. The name of each hydrocarbon ends in *-ane*.
3. The hydrocarbons from CH_4 to C_4H_{10} are gases; those from C_5 to C_{16} , liquids at ordinary temperatures; and those from C_{17} , solids.
4. The melting and boiling points increase with the increase in molecular weight.
5. The difference between any two consecutive members in this series is CH_2 .

Whenever we have a series of compounds where the difference between any two consecutive members is CH_2 , we get what is known as a **homologous** series. The word "homolog" signifies "a member of the series." Homologous series are frequently met with in organic chemistry, and we shall refer to them repeatedly. The great value in the study of these homologous series lies in the fact that members of such a series are really members of the same family and, therefore, show strong family resemblances—or, to speak in terms of chemistry, strong chemical resemblances. This does not mean that the members of a homologous series are exactly alike chemically; but it does mean that they have certain common characteristics which distinguish them from other classes of compounds. Their physical properties, too, show a regular gradation (see the table on p. 25).

6. Their type formula may be represented algebraically by $\text{C}_n\text{H}_{2n+2}$.

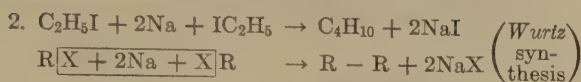
7. The names of the radicals end in *-yl*, the suffix *-ane* of the hydrocarbon being changed to *-yl* (methane \rightarrow methyl).

8. The type formula for these radicals is $\text{C}_n\text{H}_{2n+1}$ (monovalent).

9. The paraffins are known as "alkanes"; hence the radicals are spoken of as "alkyl groups." An alkyl group is often represented by the letter "R."

Lower members of the paraffin series have anesthetic properties; the higher ones, beginning with $\text{C}_{12}\text{H}_{26}$, have no physiological effects.

General Methods of Preparation.



(X refers to halogens.)

PARAFFIN SERIES (NORMAL HYDROCARBONS) *

Formula	Name	Boiling Point, °C	Melting Point, °C	Name of Mono-valent Radical	Formula of Radical
CH ₄	Methane	-161.5	-184	Methyl	CH ₃
C ₂ H ₆	Ethane	- 88.3	-172	Ethyl	C ₂ H ₅
C ₃ H ₈	Propane	- 44.5	-189.9	Propyl	C ₃ H ₇
C ₄ H ₁₀	Butane	- 0.45	-135	Butyl	C ₄ H ₉
C ₅ H ₁₂	Pentane	+ 36.2	-130	Amyl or pentyl	C ₅ H ₁₁
C ₆ H ₁₄	Hexane	+ 68.9	- 94	Hexyl	C ₆ H ₁₃
C ₇ H ₁₆	Heptane	+ 98.5	- 97	Heptyl	C ₇ H ₁₅
C ₈ H ₁₈	Octane	+125.8	- 56	Octyl	C ₈ H ₁₇
C ₉ H ₂₀	Nonane	+150.7	- 51	Nonyl	C ₉ H ₁₉
C ₁₀ H ₂₂	Decane	+174	- 32	Decyl	C ₁₀ H ₂₁
C ₁₁ H ₂₄	Undecane	+194.5	- 26.5	Undecyl	C ₁₁ H ₂₃
C ₁₂ H ₂₆	Dodecane	+214.5	- 12	Dodecyl	C ₁₂ H ₂₅
C ₁₃ H ₂₈	Tridecane	+234	- 6.2	Tridecyl	C ₁₃ H ₂₇
C ₁₄ H ₃₀	Tetradecane	+252.5	+ 5.5	Tetradecyl	C ₁₄ H ₂₉
C ₁₅ H ₃₂	Pentadecane	+270.5	+ 10	Pentadecyl	C ₁₅ H ₃₁
C ₁₆ H ₃₄	Hexadecane	+287.5	+ 19	Hexadecyl	C ₁₆ H ₃₃
C ₁₇ H ₃₆	Heptadecane	+303	+ 22.5	Heptadecyl	C ₁₇ H ₃₅
.
.
.
C ₆₀ H ₁₂₂	Hexacontane	+101	Hexacontyl	C ₆₀ H ₁₂₁
.
.
.
C _n H _{2n+2} †	Alkane	Alkyl	C _n H _{2n+1}

* A fairly complete table is given at this point to illustrate to what extent a series has been investigated. In the other portions of the book where tables will be given, only the first few members of a series will be included.

† So far the largest molecule of this series which has been prepared has the formula C₉₄H₁₉₀.

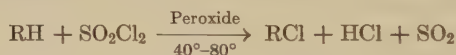
General Physical Properties. The paraffins are insoluble in, and lighter than, water, and soluble in alcohol, ether, chloroform, benzene, etc. As a rule, their odor is rather pleasant. They are flammable.

General Chemical Properties. All the paraffins are relatively stable and inert. At ordinary temperature they are not acted upon by nitric, sulfuric, hydrochloric, or chromic acids, or sodium hydroxide. However, the paraffins can be nitrated in the *vapor phase* to produce nitro-paraffins with the same number of carbon atoms together with other nitroparaffins having a shorter carbon chain. Methane is the exception, for when methane is nitrated the only nitroparaffin which can be formed is nitromethane. When ethane is nitrated, both nitroethane and nitromethane are produced. Propane is the lowest member of the paraffin series which on nitration yields both a 1- and 2-nitro compound. Thus, when propane is nitrated, there are formed 1-nitropropane, 2-nitropropane, nitroethane, and nitromethane.

The formula for nitromethane is $\text{CH}_3 \cdot \text{N} \begin{array}{l} \nearrow \text{O} \\ \searrow \text{O} \end{array}$. The nitro group is $\begin{array}{c} \nearrow \text{O} \\ -\text{N} \searrow \text{O} \end{array}$.

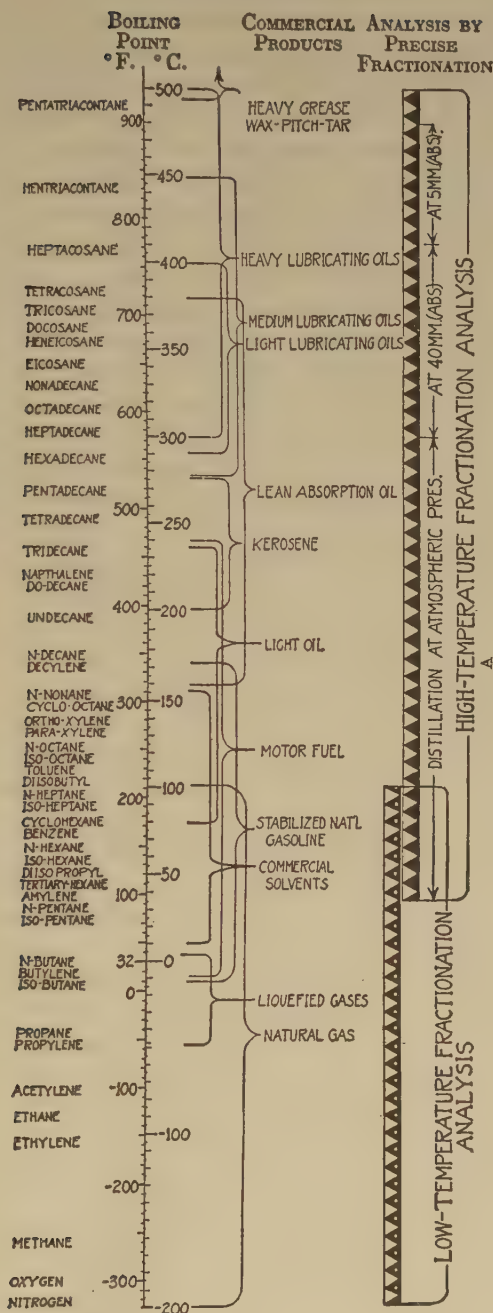
The nitroparaffins are very reactive and can be used for the preparation of many aliphatic compounds.

Normal paraffins are readily isomerized in the presence of a catalyst (AlCl_3), at room temperature, to branched-chain structures. Under proper conditions, the paraffins can be quite reactive. For example, they can be chlorinated at a relatively low temperature with sulfuryl chloride in the presence of small quantities of organic peroxides.



Chlorine reacts in sunlight to form substitution products. Bromine reacts less readily. Iodine does not react at all. (The student will be puzzled at this point to explain how the various iodide compounds used in the *Wurtz* synthesis for paraffins are prepared. We must refer him to the chapters on unsaturated hydrocarbons and alcohols for an answer.)

Petroleum or Crude Oil. The history of the development of the petroleum industry in the United States is instructive. The Indians in western Pennsylvania first discovered oil floating on surface waters. By them it was used as a remedy for all physical ills. In the middle of the last century, it occurred to a Colonel Drake that, since oil came to the surface of springs, it was probably present in much larger quantities beneath the earth's surface. He thereupon proceeded to drill a well



near Oil Creek, Pa., and, before he had dug 100 feet, oil came to the surface in such quantities that not all of it could be collected.

The industrial importance of petroleum is recognized the world over. Coal alone takes precedence over it as a fuel. It is largely, though not entirely, made up of hydrocarbons, but not all the hydrocarbons belong to the paraffin series—the series we have studied in the present chapter. Some of them belong to types of hydrocarbons with which we shall become acquainted in the next and in later chapters.

Petroleum is found in many parts of the world, but more particularly in the United States (Pennsylvania, California, and Texas), Mexico, Russia (the Baku region), Rumania, Arabia, and Persia. The natural product is usually dark in color, with a characteristic odor, and with a specific gravity that is usually, but not always, less than that of water. It may be regarded as a mixture of substances, mostly hydrocarbons.

The various products derived from petroleum are obtained by means of fractional distillation, the first fraction consisting of products which pass into the distillate up to about 200°F ; the second, those that pass over between 200° and 275° ; and the third, those that pass over above 275° . Each fraction is again redistilled and divided into more fractions, ultimately yielding substances of commercial value. In many refineries the division into fractions is based on specific gravity.

The light oils (up to 200°) include petroleum ether or ligroin, gasoline, or benzene; the illuminating oils (from 200° to 275°) include kerosene; and the lubricating oils (275° and up) include spindle, machine, and cylinder oils. In addition, many products of commercial value are obtained, such as Vaseline and paraffin wax; and the tar residue in the still is used in road-making, artificial asphalt, and roofing. If the temperature is high enough, petroleum coke is formed in the place of tar. Owing to its high purity, this coke finds extensive use in the manufacture of electrodes.

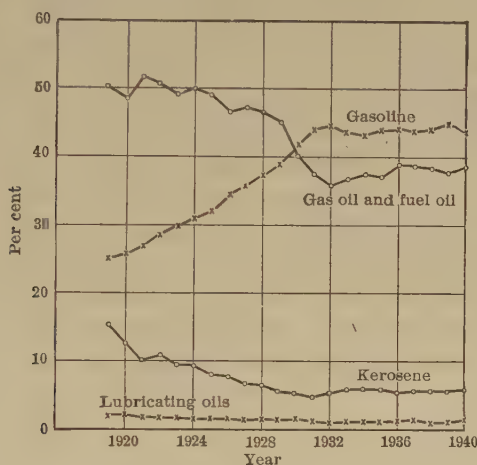
The chart on p. 27 outlines the salient features of petroleum refining and names the important products obtained.

Commercially, the most important product obtained from petroleum is gasoline (see graph), a mixture of hydrocarbons of relatively low molecular weight, such as pentane, hexane, heptane, etc. The process of purification consists of treating the gasoline with sulfuric acid (if the content of sulfur compounds is high) to remove many objectionable impurities, the sulfuric acid in turn being removed by washing with water and subsequently with sodium hydroxide solution.

The "octane number" of a gasoline is a measure of anti-knock value; its determination involves the use of two substances, *n*-heptane and iso-octane (2,2,4-trimethylpentane). When *n*-heptane is burned in a gasoline engine it knocks badly; iso-octane, on the contrary, can be made

to knock only with great difficulty. By mixing the two in the proper proportions, therefore, the knocking tendency of any ordinary fuel may be duplicated. Gasoline with an octane number of 72 has a knocking tendency equal to that of a mixture of 72 per cent of isoöctane and 28 per cent of *n*-heptane.

The very valuable isoöctane is made by combining isobutane with isobutylene (p. 38) in the presence of concentrated sulfuric acid. The process is called "alkylation."



Yields of Petroleum Fractions

Constant improvements in refinery processes have raised the octane number of gasoline steadily until now 100-octane gasoline is the normal aviation fuel, at least for military use. As a matter of fact, modern aviation fuels are mixtures, or blends, of natural and chemically produced hydrocarbons. Compounds and mixtures are being made and used which yield power much greater than that of 100-octane fuels.

The number "100-octane" represents only a theoretical maximum, estimated some years ago, which has been far exceeded by practical achievements. For instance, "triptane" (2,2,3-trimethylbutane) is being made catalytically from simpler paraffins and is reported to have 1.5 times the power of isoöctane (*Ipatieff*).

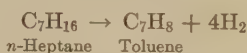
By a careful study of the reactions involved, American chemists have developed methods of increasing the yield of gasoline. The **cracking** process, used so extensively today, consists in breaking up, at high temperatures and pressures, the more complex into the simpler hydrocarbons possessing high anti-knock qualities; for example,



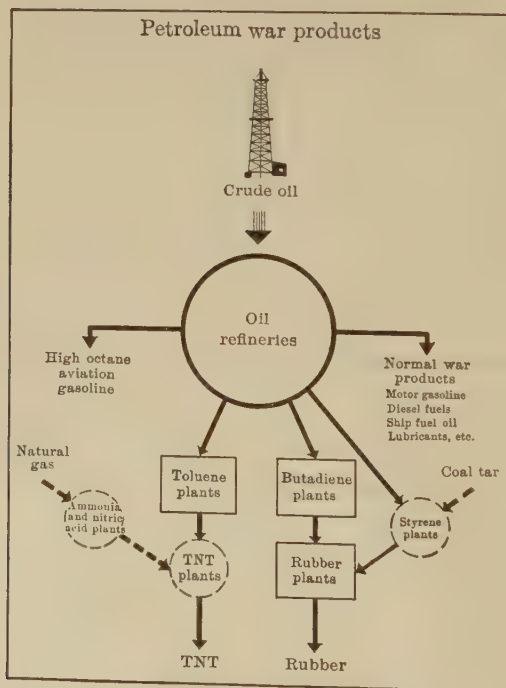
In this way gas oil is converted into the simpler hydrocarbons. At the present time approximately one-half of the gasoline produced is derived from the cracking of heavy oils. Gasolines made by the cracking process differ in composition from natural gasoline in that they contain olefins, diolefins, cyclic mono- and diolefins, aromatic compounds, etc.

Sometimes it is advantageous to build up higher-molecular-weight hydrocarbons from those of lower molecular weight. In this way gaseous by-products from cracking and refining are built up (polymerization and alkylation) into liquids falling within the gasoline boiling range.

Furthermore, paraffins are converted to cyclic aromatic hydrocarbons under proper catalytic conditions. By this so-called **hydroforming** process, *n*-heptane from petroleum has provided much of the toluene used to make TNT, a vital war weapon:

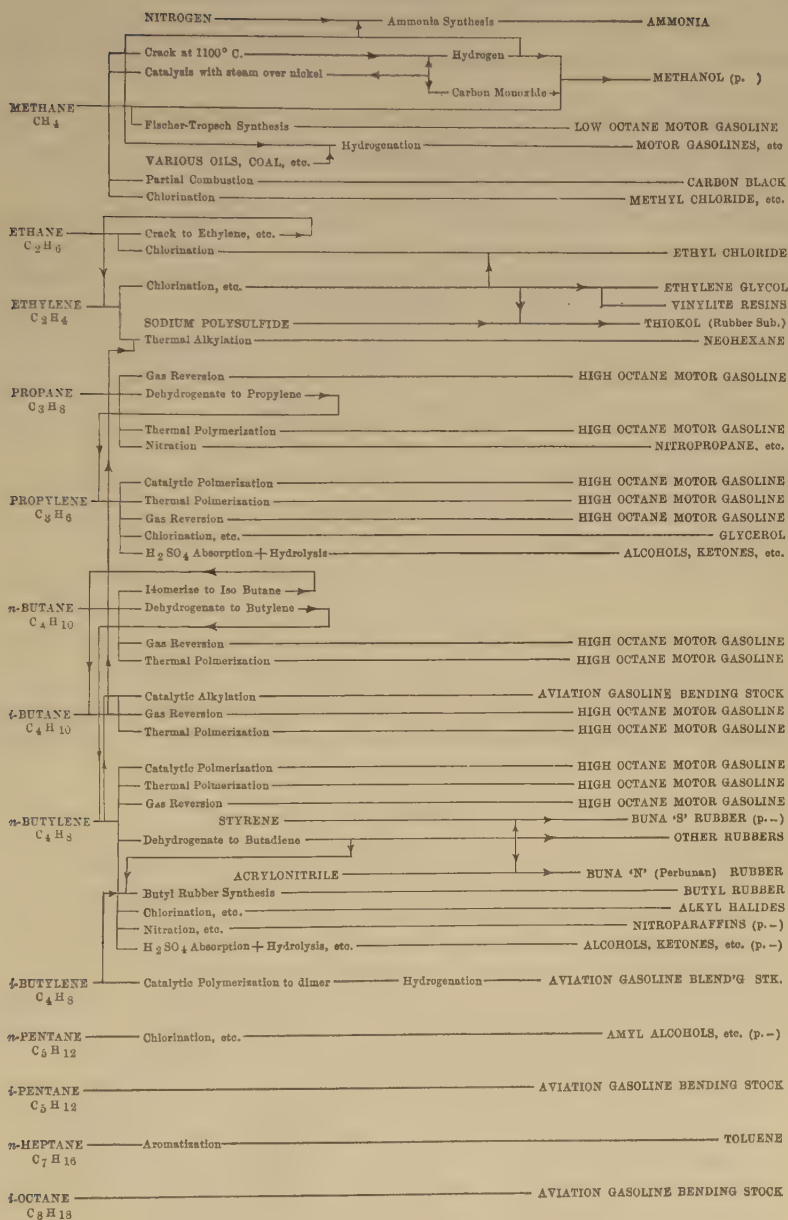


(At one time toluene had been obtained solely from the distillation of coal tar. Now much of this compound is obtained from petroleum. In fact, petroleum is the source not only of toluene but also of aviation gasoline and synthetic rubber. See the figure below.)



[F. J. Van Antwerpen, *Chemical and Engineering News*, 21, 951, 1943.]

PRODUCTS OF PETROLEUM REFINING



[Armistead, Jr., Petroleum Refining, Foster Wheeler Corp.]

By the *Bergius* process for the "liquefaction of coal," 50 to 60 per cent of the coal can be transformed into oil by hydrogenation under high pressure; and the *Fischer* process produces hydrocarbons from carbon monoxide and hydrogen at atmospheric pressure and at a relatively low temperature.

Albolene, Nujol, and petrolatum (Vaseline) are petroleum products used extensively in medicine as intestinal lubricants and in pharmacy as bases for ointments, salves, etc.

Natural gas (see chart facing p. 80), a mixture of the lower paraffins, is an important source of these hydrocarbons. In some parts of the country, it is an important fuel of high calorific value and also provides much casinghead gasoline. (Gasoline recovered from the gas that comes from a producing oil well is known as "casinghead" gasoline.) In some Texas fields, natural gas contains 1–2 per cent of helium, which the United States government recovers and uses.

Natural gas can be cracked to carbon black, used by the rubber industry, and to hydrogen, needed for the synthesis of ammonia, etc.

Natural gas, rich in methane, can be converted catalytically to water gas, which, in turn, can be converted to liquid hydrocarbons. It can be oxidized to formaldehyde and converted to acetylene at high temperatures.

To indicate the tremendous commercial possibilities of some of these hydrocarbons—obtained from natural gas and from refinery gases originating with petroleum—we append a suggestive summary on page 31 (ethylene, propylene, and butylenes are discussed in the next chapter).

QUESTIONS

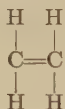
1. Indicate what is meant by the following: (a) saturated hydrocarbon; (b) paraffin; (c) homologous series; (d) alkane; (e) alkyl group; (f) substitution; (g) isomerism; (h) *Wurtz* synthesis; (i) cracking; (j) fractional distillation; (k) octane number; (l) liquefaction of coal; (m) hydroforming; (n) alkylation.
2. Compare the relative reactivity of the halogens towards methane.
3. Write structural formulas for: (a) methylmethane; (b) ethylethane; (c) dimethylmethane; (d) *n*-propyldiethylmethane; (e) trimethylmethane; (f) 2-methylpropane; (g) 1-methyl-3-*n*-propylpentane; (h) 1,1-diethylbutane; (i) methyl bromide; (j) *n*-propyl iodide; (k) 2,3-dimethylbutane; (l) *n*-butane; (m) isopentane; (n) 2,2-dichloropentane; (o) neopentane; (p) 2-methyl-4-bromopentane; (q) *sym*-diethylethane; (r) *unsym*-dimethylethane; (s) *sym*-dichloroethane; (t) methylene bromide; (u) 2,2,3-trichloropentane; (v) 2-nitropropane.
4. Write structural formulas for all the (a) butanes; (b) pentanes; (c) hexanes. Name these compounds.
5. Give two names for each of the following compounds: CHCl_3 , CH_3Cl , CH_2F_2 , C_2H_6 , CF_4 , $\text{CH}_3\text{CH}_2\text{Cl}$, C_3H_8 , and $\text{CHCl}_2 \cdot \text{CH}_2\text{Cl}$.

6. Write equations for the preparation of the following compounds:
 - (a) methane from aluminum carbide
 - (b) methane " sodium acetate
 - (c) ethane " ethyl iodide
 - (d) *n*-hexane " *n*-propyl iodide.
7. Write the structural formulas and names of all the monochloro substitution products of pentane and of all the dibromo substitution products of propane.
8. Why may *n*-butane be given any one of the following names: methylpropane, ethylethane, diethyl, *n*-propylmethane, and symmetrical dimethylethane? Why may isobutane also be called trimethylmethane and unsymmetrical dimethylmethane?
9. Write the structural formulas of all the hydrocarbons formed when a mixture of ethyl bromide and isopropyl bromide is treated with sodium.
10. Plot the boiling points and melting points of the normal paraffins against the number of carbon atoms.

CHAPTER III

UNSATURATED HYDROCARBONS: OLEFINS, ACETYLENES, DIOLEFINS

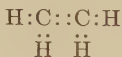
So far we have been dealing with hydrocarbons that are saturated. When bromine comes in contact with a hydrocarbon of the methane series, C_nH_{2n+2} , it can enter the compound by substitution only, not by addition; that is, by eliminating one or more hydrogen atoms from the molecule and substituting other atoms, but not by adding an outside atom without any elimination. In this chapter we take up several series of unsaturated compounds, where, as we shall see, atoms can enter the molecule without others leaving it. One series is known as the **olefins**, C_nH_{2n} , the first compound being ethylene



and another, the **acetylenes**, C_nH_{2n-2} , the first member of which is acetylene itself,



Since, according to *Lewis*, the sharing of a pair of electrons is the equivalent of the single bond, ethylene can be represented as



and acetylene as



The student must not draw the conclusion that, because there is more than one bond between two atoms, the union between such atoms is correspondingly stronger. On the contrary, since bonds represent strains, the greater the number of bonds between any two carbon atoms, the greater the strain, and hence the greater the chemical reactivity (tendency to relieve the strain) of the compound. Therefore, ethylene is more reactive than ethane, and acetylene more than ethylene.¹

¹ The instructor may illustrate these strains by means of atomic models.

OLEFIN SERIES, C_nH_{2n} —ALKENES

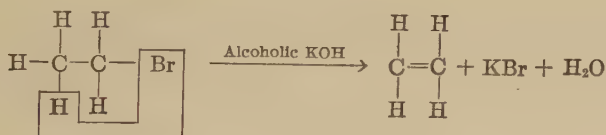
CH_2 (hypothetical)	Methylene
C_2H_4	Ethylene or ethene
C_3H_6	Propylene or propene
C_4H_8	Butylene or butene
C_5H_{10}	Amylene or pentene
etc. (Compare with the paraffins, p. 25.)	

These compounds constitute a homologous series, just like the paraffins, for there is the same difference between any two consecutive members, namely, CH_2 ; but it will be noticed that the olefins have two hydrogen atoms less than the corresponding paraffins. The simplest known member of the olefin series, ethylene, combines with chlorine to form an oil ($C_2H_4Cl_2$); hence the name **olefin** (oil-forming).

In naming these compounds in the Geneva system, we change the ending *-ane* of the paraffin containing the same number of carbon atoms into *-ene*; for example, C_2H_6 (ethane)— C_2H_4 (ethylene or ethene).

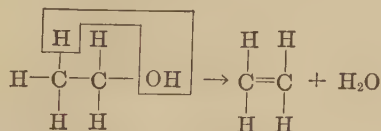
We shall describe one member of this series, ethylene, in some detail; the general characteristics of the other members can be gleaned from a study of this one.

Preparation of Ethylene, C_2H_4 . One method of preparation is by the action of an alcoholic solution of sodium or potassium hydroxide on ethyl bromide, a method that gives us an insight into the structure of the compound:

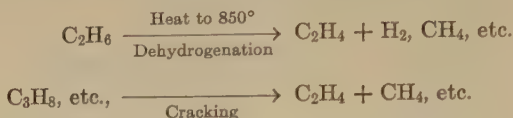


If, instead of an alcoholic solution of sodium or potassium hydroxide, we use an aqueous solution, ethyl alcohol, C_2H_5OH , is produced.

Another method is to treat ethyl alcohol with a strong dehydrating agent, such as P_2O_5 or H_2SO_4 , or to pass the vapors of alcohol over clay heated to 400° .

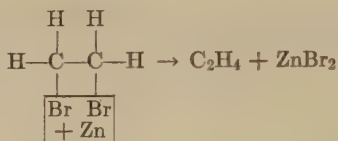


Ethylene is now obtained commercially from ethane and other components of natural gas (see chart facing p. 80):



Many homologous olefins are made similarly.

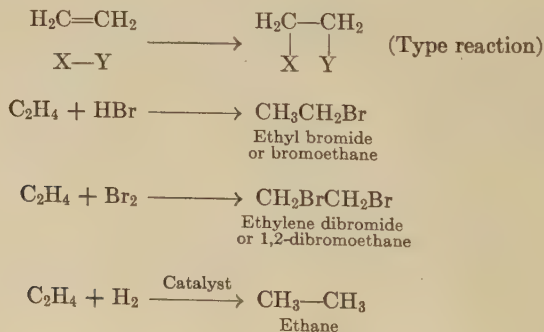
The action of sodium or zinc on ethylene bromide (1,2-dibromoethane) also yields ethylene:

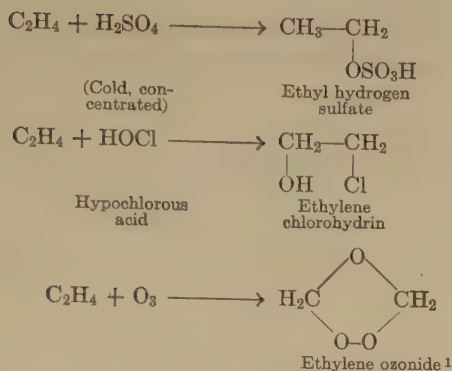


$\text{C}_2\text{H}_4\text{Br}_2$ may be regarded as ethylene, C_2H_4 , to which two bromine atoms have been added, or as ethane in which two of the hydrogens attached to different carbon atoms are replaced by bromine.

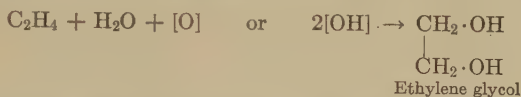
Properties. Ethylene is a colorless gas with a sweetish odor. It burns with a smoky, luminous flame and forms explosive mixtures with air. It is present in coal gas to the extent of 4–6 per cent, and is partially responsible for its luminosity. It is produced, therefore, in the destructive distillation of coal. *Luckhardt* has shown that ethylene is a powerful anesthetic and has even some advantages over nitrous oxide. Ethylene has also been introduced for coloring mature citrus fruits (oranges, lemons, etc.).

The properties of ethylene result from its unsaturated character—its double bond. It combines by addition with halogen acids, with halogens, with hydrogen, with sulfuric acid, with hypochlorous acid, with ozone, etc., and is used as the starting material for the preparation of many organic compounds (see, for example, the chart facing p. 80). Some simple reactions are the following:



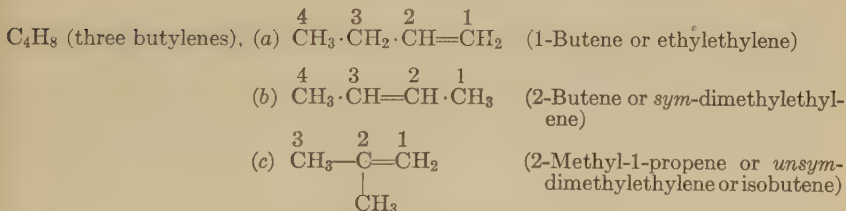
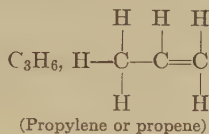


A test sometimes used for the detection of the double bond is based on the action of very dilute potassium permanganate solution; the violet color of the permanganate changes to brown, owing to its reduction. The reaction may be represented thus:

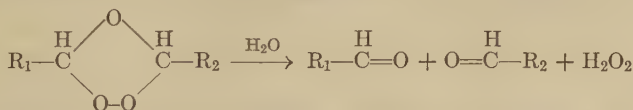


The student must clearly understand that C_2H_4 alone represents the gas ethylene, but C_2H_4 may be present as a divalent group in a compound; for example, ethylene bromide, $\text{C}_2\text{H}_4\text{Br}_2$.

Higher homologs.



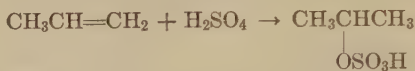
¹ The ozonides of olefins are unstable compounds, but they are valuable because, upon hydrolysis, they are split into oxygenated compounds—aldehydes and ketones—from whose structures that of the original olefin can be reconstructed:



Zinc dust, or some other reducing agent, prevents further oxidation of the products of hydrolysis to acids by the hydrogen peroxide.

Sometimes the Greek letter Δ is used to denote the double bond, so that (a), (b), and (c) may also be written Δ^1 -butene, Δ^2 -butene, and 2-methyl- Δ^1 -propene, respectively.

The methods of preparation and the properties of the higher olefins are analogous to those described for ethylene. However, in the case of unsymmetrical olefins, like $R_1CH=CHR_2$, and unsymmetrical reagents, like HX , H_2SO_4 , and $HOCl$, addition proceeds, at least for the simpler hydrocarbons, in such a way that the hydrogen or other positive fragment of the reagent adds to the carbon atom of the olefin which is richer in hydrogen (rule of *Markownikoff*). For example,

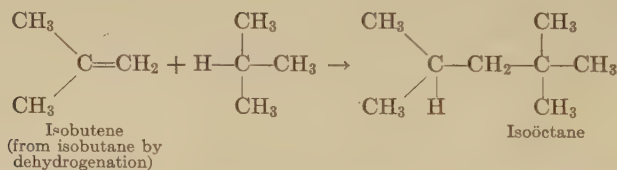


($HOCl$ adds as $OH-Cl^+$.)

With branched olefins, and at higher temperatures with the normal compounds, chlorine reacts by substitution rather than by addition.

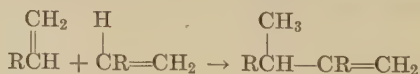


Olefins of branched structure can be saturated by the addition of paraffins under proper conditions. This **alkylation** yields hydrocarbons of high octane rating.

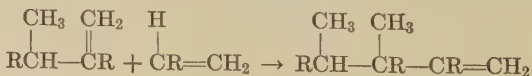


Observe that we have here another example of directed addition, described by *Markownikoff's* rule.

Applying the same principle, we can show how one molecule of an olefin partially saturates another molecule of the same substance:



The resulting olefin can add a third molecule:

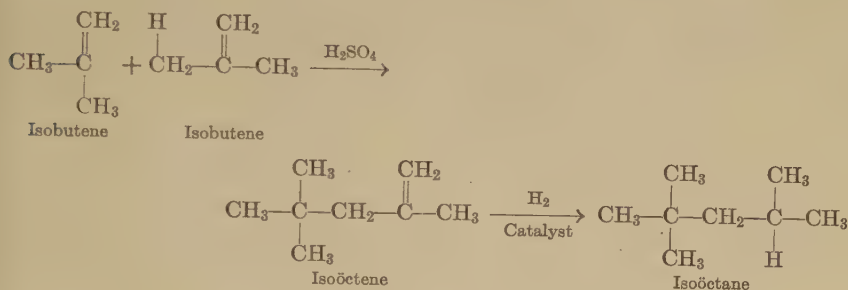


Similarly, a fourth and a fifth molecule can be added; etc. This process of **polymerization**, as it is called, may therefore be considered

an addition of simple molecules of a substance (the **monomer**) to yield polymer products, which are sometimes called more specifically **addition polymers**.

Strong acid catalysts, such as sulfuric acid, are necessary for such polymerizations. Many of these "synthetic" polymers have valuable properties equaling, and sometimes surpassing, those of the "natural" polymers, such as rubber, resins, and fibers.

In some, though by no means in all, cases, it is possible to control the polymerization, so that it can be stopped after a definite number of monomer molecules have added to each other. For example, one method of making isoöctane involves the combination (**dimerization**) of two molecules of isobutene; the reaction may be made to stop at the isoöctene stage:



ACETYLENE SERIES, $\text{C}_n\text{H}_{2n-2}$ —ALKYNES

- C_2H_2 Acetylene or ethyne
 C_3H_4 Methylacetylene or propyne
 C_4H_6 Dimethylacetylene or ethylacetylene or butyne
 etc.

These also constitute a homologous series. The members contain two hydrogen atoms less than the corresponding olefins, or four hydrogen atoms less than the corresponding paraffins. They are named in the Geneva system by changing the *-ane* ending of the paraffins into *-yne*, so that ethane, C_2H_6 , for example, becomes ethyne, C_2H_2 . This series is known as the acetylene series, for acetylene is the most important member.

As before, we shall discuss a typical member in some detail.

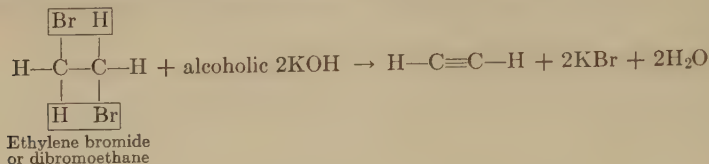
Acetylene, C_2H_2 , has the formula $\text{H}-\text{C}\equiv\text{C}-\text{H}$, which shows it to have a triple bond and therefore indicates that it is even more unsaturated than ethylene,¹ a view which is confirmed by a study of its reactions. Acetylene is an extremely reactive compound.

¹ The instructor may illustrate this by the use of atomic models.

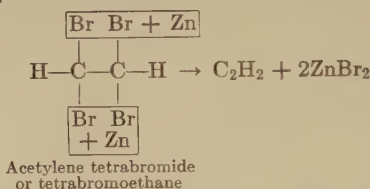
Preparation. One method is probably already familiar to the student. It is the action of water on calcium carbide:



Another is similar to a method used for the olefins:

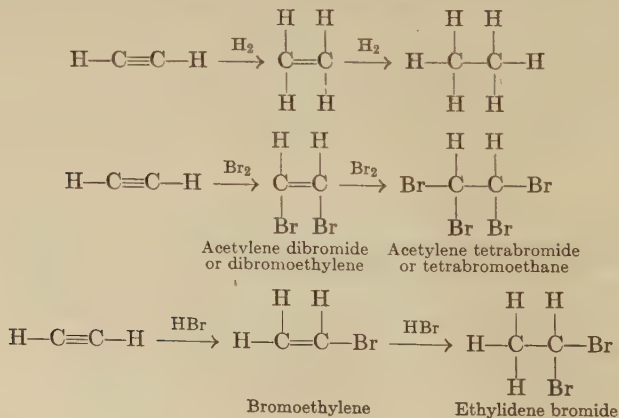


So is the following:



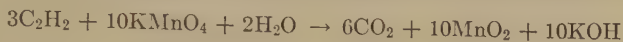
Acetylene is a colorless gas. When mixed with air in a special type of burner, it burns with a very brilliant white light and is used for illuminating purposes. When burned it gives out a large amount of heat. This is made use of in the oxyacetylene torch (for cutting steel, etc.) wherein acetylene, supplied under pressure, is burned in the presence of oxygen. The gas may explode if stored under pressure, but it can be handled safely if it is first dissolved in acetone (as in "Prestolite" tanks). Liquid acetylene is highly unstable and highly explosive.

Properties. Since acetylene is an unsaturated compound, it will form addition products (like ethylene); but since it is more unsaturated than ethylene, it can add to itself more atoms than C_2H_4 .

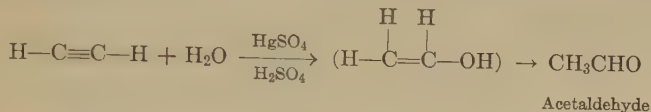


We see that the addition is directed just as in the case of the olefins. $\text{CH}_2\text{Br}\cdot\text{CH}_2\text{Br}$, ethylene bromide, or symmetrical dibromoethane, is isomeric with $\text{CH}_3\cdot\text{CHBr}_2$, ethylidene bromide, or unsymmetrical dibromoethane.

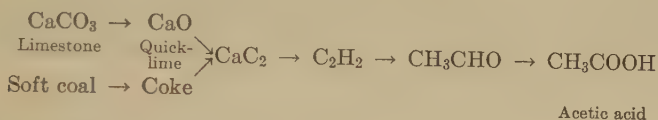
Acetylene also reacts with dilute potassium permanganate solution:



In the presence of mercuric sulfate in dilute sulfuric acid, acetylene adds on water:

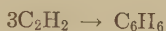


As we shall see, acetaldehyde is easily oxidized to acetic acid, and, therefore, this reaction is a step in the synthesis of an important substance from naturally occurring materials:

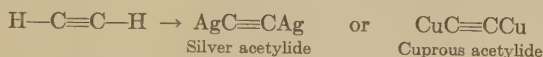


The student must clearly understand that C_2H_2 alone represents the gas acetylene, but C_2H_2 may be present as a divalent group in a compound; for example, acetylene dibromide, $\text{C}_2\text{H}_2\text{Br}_2$. It may also be present as a tetravalent group; for example, acetylene tetrabromide, $\text{C}_2\text{H}_2\text{Br}_4$.

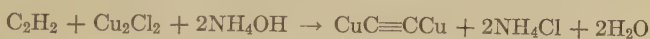
When acetylene is passed over finely divided nickel, three molecules of it polymerize to form benzene:



Acetylene combines with ammoniacal silver chloride or cuprous chloride solution to form insoluble metallic derivatives (acetylides).

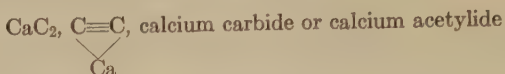


The reaction may be expressed as follows:



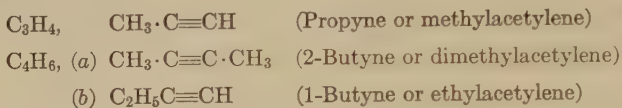
This reaction offers a simple method of distinguishing between many acetylenes and the olefins. Both groups are unsaturated towards bromine water and aqueous potassium permanganate, but only acetylene and monosubstituted acetylenes yield the insoluble acetylides.

Many acetylides are highly unstable and explosive, particularly in the dry state. In fact, many of the explosions involving acetylene are due to the formation of these acetylides.



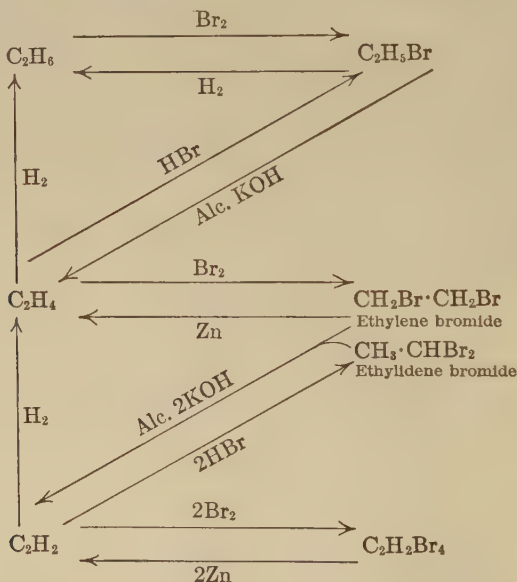
The hydrogen attached to acetylenic carbons is also acidic toward (is replaced by) active metals like sodium, potassium, and calcium, in the molten state or in liquid ammonia.

Higher homologs.



The general properties correspond to those of acetylene, except that only the compounds with the structure $\text{—C}\equiv\text{C—H}$ can form acetylides. Addition reactions proceed according to *Markownikoff's* rule.

The following diagram makes clear some of the interconnections of compounds already discussed.

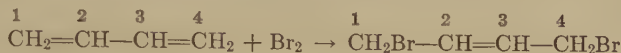


DIOLEFINS (DIENES), $\text{C}_n\text{H}_{2n-2}$

Compounds containing two double bonds are isomeric with those containing one triple bond; for example, $\text{CH}_3\text{—C}\equiv\text{CH}$ is isomeric with

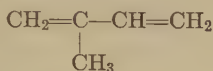
$\text{CH}_2=\text{C}=\text{CH}_2$. The name of a compound having one double bond ends in *-ene*; the name of a compound having two double bonds has the ending *-diene*; e.g., $\text{CH}_2=\text{C}=\text{CH}_2$ is propadiene. Butadiene is $\text{CH}_2=\text{CH}-\text{CH}=\text{CH}_2$.

This arrangement of two double bonds separated by one single bond is a stable configuration, as evidenced by its frequent occurrence in many types of natural products. It is called a *conjugated* double bond system, and it exhibits its stability by sometimes reacting as a single unit, as, for instance, in the addition of bromine:



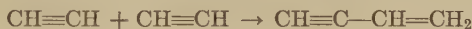
This is generally known as *1,4 addition*.

An important diolefin is **isoprene**,



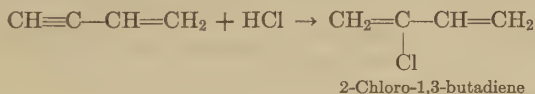
or 2-methyl-1,3-butadiene, which has been shown to be one of the decomposition products of caoutchouc (natural rubber), and which can be obtained by the distillation of the latter. Isoprene itself (in the presence of catalysts, as HCl, Na, etc.) has been polymerized back into a substance resembling caoutchouc, the resulting product showing some striking resemblances to natural rubber.

Acetylene may be polymerized to vinylacetylene by the use of a saturated aqueous solution of cuprous chloride and ammonium chloride as catalyst:



The $\text{CH}_2=\text{CH}$ monovalent group is known as the vinyl group.

When vinylacetylene (a $\text{C}_n\text{H}_{2n-4}$ hydrocarbon) is treated with hydrogen chloride, **chloroprene** is obtained:



The chloroprene, allowed to stand at room temperature and in the absence of direct light, gradually polymerizes to a stiff, pale yellow, elastic mass which resembles a completely vulcanized soft rubber (Neoprene).

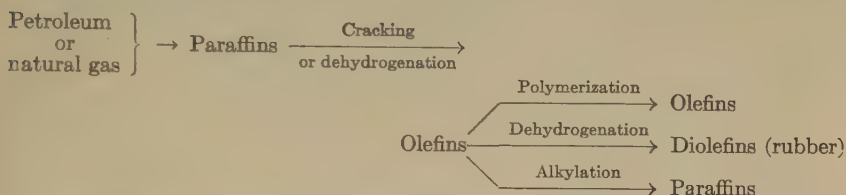
Some of the notable achievements of chemistry in recent years have been largely the result of war activities, among the most striking being the development of **synthetic rubbers**, of which Neoprene is an example. Practically all of them are polymers (*elastomers*) of either 1,3-butadiene, or some homolog or derivative which contains the same conjugated

(Acrylonitrile has the formula $\text{CH}_2=\text{CH}-\text{CN}$; see p. 185. The formula for

styrene is $\text{C}_6\text{H}_5\text{CH}=\text{CH}_2$, see p. 242). Still another variety of synthetic rubber, Thiokol, is referred to on p. 215.

Thus we see that unsaturated hydrocarbons are the primary substances from which most, if not all, of our rubber will soon be made. This means, too, that petroleum assumes even greater prominence as a source of raw materials for indispensable commodities.

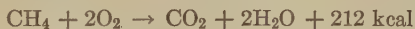
The interconnections among the various families of hydrocarbons may be summarized thus:



It must be remembered, however, that butadiene, the key compound in rubber synthesis, is also made from ethyl alcohol, which in turn is obtained from products of agriculture; so that farmers also are interested in the development of a synthetic-rubber industry, even if we exclude the possibility of developing the cultivation of plants which yield a satisfactory natural rubber, like guayule and Russian dandelion.

THERMOCHEMISTRY OF THE HYDROCARBONS

Substances containing carbon and hydrogen—organic compounds in general—evolve a considerable quantity of heat when burned (*exothermic* reaction). Hydrocarbons exhibit this property. Such *heats of combustion*, which can be measured in a calorimeter, are expressed as kilogram calories (kcal) per mole. For example, when methane is burned the reaction may be written



In this way the fuel value of coal, of gasoline, of foodstuffs, etc., can be determined.

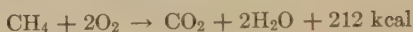
The heats of combustion of ethylene and acetylene are 332 and 312 kcal, respectively.

Now acetylene, C_2H_2 , has a heat of combustion (312) which is not so very much less than that of ethane, C_2H_6 (370), despite the fact that ethane has four more hydrogen atoms and would therefore be expected to produce considerably more heat than acetylene when burned.

This suggests that the acetylene molecule has a comparatively large potential energy. In order to determine such potential (or storage) energy we determine the *heat of formation* of the compound, that is, the amount of heat liberated (exothermic) or absorbed (endothermic) when the elements—in this case carbon and hydrogen—unite to form the compound.

Unfortunately, it is practically impossible to get the heat of formation of acetylene, say, by causing carbon and hydrogen to combine. Carbon and hydrogen do *not* combine to form acetylene. In general, the heats of formation of organic compounds are obtained indirectly by subtracting the heat of combustion of the compound from the heat of combustion of the same amounts of carbon and hydrogen. One or two examples will be given.

We have said that, when methane burns,



Now, when carbon is burned,



and when hydrogen is burned,



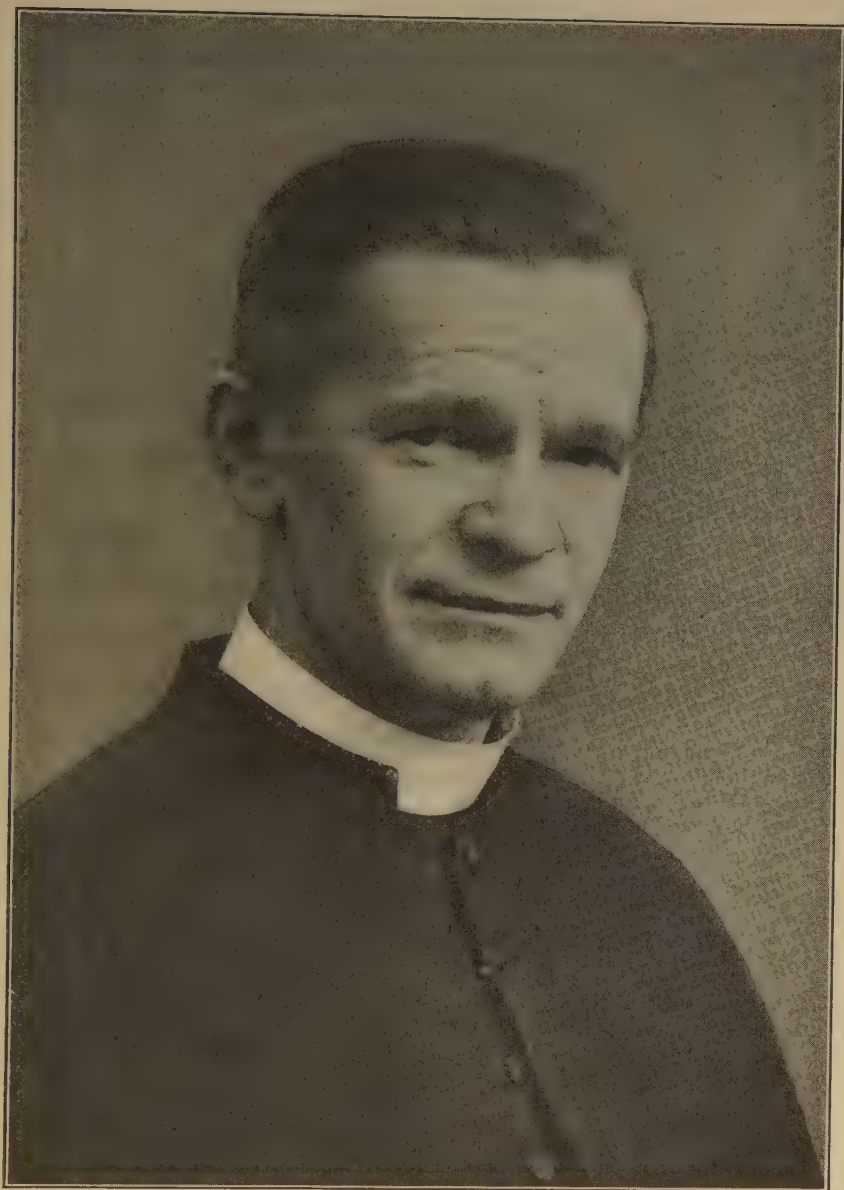
But, since $2\text{H}_2\text{O}$ are evolved when methane is burned, we double the last figure: $68 \times 2 = 136$.

This means that when 12 grams of carbon (C) and 4 grams of hydrogen (2H) burn, the total amount of heat produced is $94 + 136 = 230$ kcal. On the other hand, as we have seen, in the combustion of methane 212 kcal is evolved. If, therefore, carbon and hydrogen were to unite to form CH_4 , the heat liberated would be $230 - 212 = 18$ kcal, which is, therefore, the heat of formation of methane. Since heat is given off, the reaction is exothermic.

If we go through the same reasoning for acetylene, we find that



We have already seen that, when carbon burns, 94 kcal is evolved. Since in the above reaction 2CO_2 are involved, the figure 94 would have to be doubled: 188. The hydrogen when burned liberates 68 kcal. The total is therefore 256 kcal. But 256 kcal is 56 kcal *less* than when acetylene is burned ($312 - 256$), which means that heat would be *absorbed* in the union of carbon and hydrogen to form acetylene. Hence the heat of formation of acetylene is -56 kcal; and this represents an endothermic reaction.



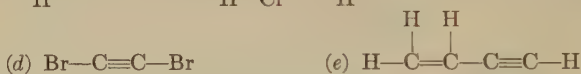
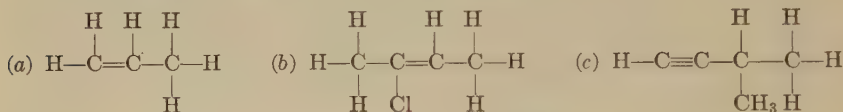
JULIUS A. NIEUWLAND (1876-1936)

Professor at Notre Dame University, whose extensive work on acetylene derivatives led to the synthesis of Neoprene. He received the Nichols medal in 1935.

The heat of formation of ethane = 23 kcal; ethylene = -14 kcal; acetylene = -56 kcal. These facts can be correlated with the chemical reactivities of these types of hydrocarbons.

QUESTIONS

1. Indicate what is meant by the following: (a) unsaturated hydrocarbon; (b) alkene; (c) alkyne; (d) diene; (e) olefin.
2. Indicate the reactions involved in converting ethylene into ethylidene bromide.
3. Write structural formulas for: (a) propylene; (b) propyne; (c) *sym*-dimethylethylene; (d) methylacetylene; (e) *unsym*-diethylethylene; (f) ethyl-*n*-propylacetylene; (g) dichloroacetylene; (h) bromoethene; (i) 1-butene; (j) 2-pentene; (k) 2-hexyne; (l) 1-ethyl-2-pentene; (m) 1-chloro-1-butene; (n) ethylene chloride; (o) ethylidene bromide; (p) acetylene dibromide; (q) silver acetylide; (r) ethylene ozonide; (s) chloroprene; (t) 2-methyl-1,3-butadiene; (u) 1,5-hexadiyne.
4. Write at least one name for each of the following:



5. Write equations for the preparation of the following compounds:

(a) ethylene	from ethyl alcohol.
(b) ethylene	" acetylene
(c) acetylene	" ethylene bromide
(d) propylene	" propyl chlorides
(e) propylene	" propylene chloride
(f) vinylacetylene	" acetylene
(g) chloroprene	" acetylene
(h) 1-butyne	" 2-bromobutane
6. What characteristic group is present in acetylenes which yield acetylides?
7. Complete the following equations, and name the organic compounds produced

(a) $\text{C}_2\text{H}_2 + 2\text{HI} \rightarrow$	(f) $\text{C}_2\text{H}_2 + 2\text{Br}_2 \rightarrow$
(b) $\text{C}_2\text{H}_4 + \text{HOCl} \rightarrow$	(g) $\text{C}_2\text{H}_4 + \text{O}_3 \rightarrow$
(c) $\text{C}_2\text{H}_2 + 2\text{HBr} \rightarrow$	(h) isoprene + $\text{Br}_2 \rightarrow$
(d) $\text{C}_3\text{H}_6 + \text{HI} \rightarrow$	(i) butene + dil. aq. $\text{KMnO}_4 \rightarrow$
(e) $1\text{-butene} + \text{H}_2\text{SO}_4 \rightarrow$	(j) propyne + $\text{Cu}_2\text{Cl}_2(\text{NH}_3) \rightarrow$
8. Write the possible structural formulas of a polymer of chloroprene.
9. Write all possible structural formulas for C_6H_8 .

CHAPTER IV

HALOGEN DERIVATIVES OF HYDROCARBONS

We have already observed that the action of chlorine on methane gives us the following substitution products: CH_3Cl , CH_2Cl_2 , CHCl_3 , and CCl_4 . It ought to be possible to prepare any one of these substances by employing the proper amount of chlorine, and the supply of methane from petroleum is plentiful. In practice, however, it is found that a series of simultaneous reactions occurs, yielding a mixture of chlorides. Mention may be made at this point of the many attempts to produce chloroform, CHCl_3 , on a commercial scale by the action of chlorine on methane, and also of the attempts to make methyl chloride, CH_3Cl , by a similar reaction. Methyl chloride can be easily hydrolyzed to methanol or wood alcohol, CH_3OH , and thus the synthetic methanol can be prepared starting from natural gas, which contains methane.

Bromine is less reactive than chlorine; it produces analogous substitution products. Iodine does not react with methane.

Monohalogen Derivatives of the Paraffins. An alkyl halide (or monohalogen derivative of a hydrocarbon) may be regarded as a saturated hydrocarbon in which one of the hydrogens is replaced by a halogen (F, Cl, Br, I). The following will make this clear:

$\text{C}_n\text{H}_{2n+2}$	$\text{C}_n\text{H}_{2n+1}$ Group	$\text{C}_n\text{H}_{2n+1}\text{X}$ (alkyl halide)
Methane, CH_3H	Methyl group, CH_3	Methyl chloride, CH_3Cl
Ethane, $\text{C}_2\text{H}_5\text{H}$	Ethyl group, C_2H_5	Ethyl bromide, $\text{C}_2\text{H}_5\text{Br}$
etc.	etc.	etc.
Alkane, RH	Alkyl group, R	Alkyl halide, RX

(RX is the type formula for an alkyl halide.)

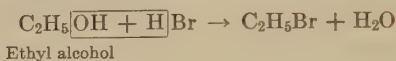
ALKYL HALIDES

Chloride	For- mula	B.P. °C	Bromide	For- mula	B.P. °C	Iodide	For- mula	B.P. °C
Methyl	CH_3Cl	-24	Methyl	CH_3Br	4.5	Methyl	CH_3I	43
Ethyl	$\text{C}_2\text{H}_5\text{Cl}$	12.5	Ethyl	$\text{C}_2\text{H}_5\text{Br}$	38.4	Ethyl	$\text{C}_2\text{H}_5\text{I}$	72
Propyl	$\text{C}_3\text{H}_7\text{Cl}$	46.5	Propyl	$\text{C}_3\text{H}_7\text{Br}$	71	Propyl	$\text{C}_3\text{H}_7\text{I}$	102
Isopropyl	$\text{C}_3\text{H}_7\text{Cl}$	36.5	Isopropyl	$\text{C}_3\text{H}_7\text{Br}$	59	Isopropyl	$\text{C}_3\text{H}_7\text{I}$	89
n-Butyl	$\text{C}_4\text{H}_9\text{Cl}$	77.5	n-Butyl	$\text{C}_4\text{H}_9\text{Br}$	101	n-Butyl	$\text{C}_4\text{H}_9\text{I}$	129
etc.			etc.			etc.		

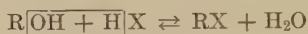
In each group the specific gravities decrease as the molecular weights increase. The specific gravity increases as we pass from a certain alkyl chloride to the bromide and in turn to the iodide having the same alkyl group.

These halides are insoluble in water but soluble in ether, benzene, and alcohol. The halides are generally colorless liquids with a pleasant odor. On standing, they develop color (this is especially true of the iodides) as a result of decomposition, and they are generally kept in amber-colored bottles.

General Methods of Preparation. The monohalides can be made by the action of a halogen acid on an alcohol in presence of a dehydrating agent. (An alcohol contains the —OH group: $\text{C}_2\text{H}_5\text{OH}$, ethyl alcohol, $\text{C}_3\text{H}_7\text{OH}$, propyl alcohol, and in general ROH .)



Or, more generally,

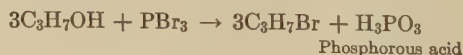
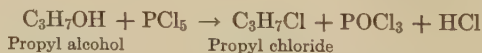


Whenever, throughout the text, “R” is used in an equation, it implies that the reaction is a general one, or, in other words, a “type” reaction. This does not necessarily mean that where specific examples are given they cannot illustrate general type reactions. As a matter of fact, most of the specific examples do illustrate type reactions.

The reaction just given seems analogous to the “neutralization” reaction in inorganic chemistry, such as $\text{Na}\boxed{\text{OH} + \text{H}}\text{Cl} \rightarrow \text{NaCl} + \text{H}_2\text{O}$. However, the production of NaCl is an instantaneous reaction, whereas the formation of RX is a comparatively slow process; and in the production of RX a dehydrating agent must be present to remove the water as fast as it is formed; otherwise the reaction is reversible.

With hydrogen iodide poor yields are obtained, owing to the fact that HI is a powerful reducing agent. With hydrogen chloride, anhydrous zinc chloride is generally used as a dehydrating agent.

Another method is the action of a phosphorus halogen compound on an alcohol; e.g.,

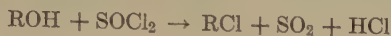


OR

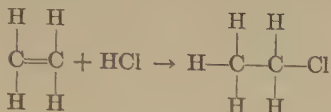


To prepare bromides or iodides it is sufficient to treat an alcohol with red phosphorus and the halogen.

Chlorides are also made conveniently with thionyl chloride:



A third method consists in the addition of halogen acids to unsaturated compounds; e.g.,



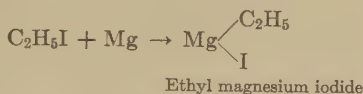
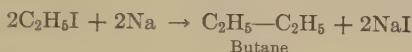
or



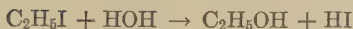
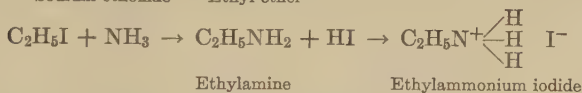
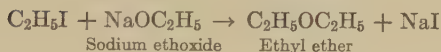
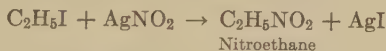
Direct halogenation of paraffins is, as we have already seen (p. 49), an unsatisfactory laboratory method, though on a commercial scale it has proved feasible (p. 71).

Properties. The halogen compounds react with many reagents to form diverse products. The following are examples of a number of type reactions.

The *Wurtz* synthesis:



Such compounds are known as *Grignard* reagents, the general type formula being $\text{R} \cdot \text{Mg} \cdot \text{X}$.



At this stage the student is not expected to memorize these equations, but rather, by examining them, to understand why the halides find such extensive applications.

Many of the reactions illustrated are of the "double decomposition" type.

Methyl chloride, CH_3Cl , and **ethyl chloride**, $\text{C}_2\text{H}_5\text{Cl}$, are used as local anesthetics, for when sprayed upon the skin the liquids evaporate rapidly, thereby cooling the tissues. They are also used for refrigerating purposes.

Two processes are used for the large-scale production of methyl chloride: the action of chlorine on methane, and the reaction of hydrochloric acid with methyl alcohol in the presence of a catalyst:

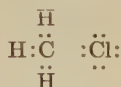


Where purity is of importance, this second method is to be preferred; the first method, the action of chlorine on methane, yields not only methyl chloride but also methylene chloride, chloroform, and carbon tetrachloride, and it is very difficult to avoid the formation of such mixtures.

Methyl chloride cannot be regarded as a purely non-polar combination, such as methane or ethane. It is a fact, for example, that methyl chloride combines with water—slowly, to be sure—to form H^+ and Cl^- .

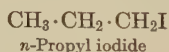


The formation of a chloride ion presupposes a transfer rather than a sharing of an electron; and we may indicate this by showing the electrons between C and Cl as being closer to Cl than to C:



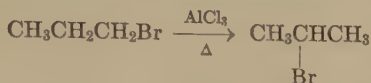
Since chlorine is an oxidizing agent, methyl chloride may be regarded as an oxidation product of methane.

Ethyl chloride is used in the preparation of lead tetraethyl and of diethylaniline. Ethyl bromide, $\text{C}_2\text{H}_5\text{Br}$, has also been used as an anesthetic.

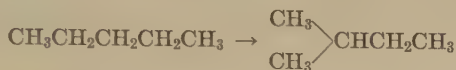


Amyl chlorides, $\text{C}_5\text{H}_{11}\text{Cl}$, are used in organic syntheses to introduce the amyl radical. A mixture of these is obtained by the chlorination of the pentanes from petroleum or natural gas.

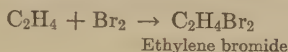
An interesting type of reaction is illustrated by the catalytic effect of anhydrous aluminum chloride on normal halides:



This is a simple example of **molecular** (intramolecular) **rearrangement**, which also occurs in similar fashion with normal paraffins to yield so-called isoparaffins of greater anti-knock value; for instance:



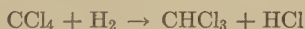
Dihalogen Derivatives of the Paraffins. Dihalogen derivatives of the paraffins have the general formula $\text{C}_n\text{H}_{2n}\text{X}_2$. ($\text{C}_2\text{H}_4\text{Br}_2$, dibromoethane, and $\text{C}_3\text{H}_6\text{Cl}_2$, dichloropropane, are examples.) They are usually prepared by the addition of a halogen to an unsaturated hydrocarbon:



Methylene iodide, CH_2I_2 , is of interest since it is the heaviest organic liquid, its specific gravity being 3.292 at 18° ; ethylene chloride, $\text{CH}_2\text{Cl}-\text{CH}_2\text{Cl}$, is used as a fumigant and also as a solvent for oils, fats, etc., and for the preparation of ethylene glycol. Ethylene bromide is used as an ingredient of anti-knock agents for motor fuels; it supplies the bromine which forms the volatile PbBr_4 which is eliminated in the exhaust. For this purpose so much bromine is required that it has to be extracted from sea water.

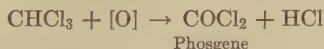
Trihalogen Derivatives of the Paraffins. The important compounds of this type are chloroform, CHCl_3 ; bromoform, CHBr_3 ; and iodoform, CHI_3 .

Chloroform can be prepared by the action of chlorine and a base on ethyl alcohol or acetone. It is now made on a large scale by the reduction of CCl_4 with moist iron:



Chloroform (trichloromethane) (b.p. 61°) is a colorless liquid with a sweet taste and suffocating odor. It is slightly soluble in water and is non-flammable. Its anesthetic properties were discovered by Dr. *Simpson* of Edinburgh in 1848.

Chloroform has a tendency to decompose when exposed to air and light:



To prevent decomposition, ethyl alcohol (to the extent of about 1 per cent) is added to the chloroform. Chloroform is usually kept in amber-colored bottles.

Pure CHCl_3 does not react with silver nitrate, but, if any decomposition has occurred, a precipitate of AgCl forms.

CHCl_3 alone is now rarely used as an anesthetic, for ether and ethylene have largely taken its place. Sometimes a mixture of ether and chloroform is used. The advantages of ether over chloroform are that it is less dangerous and that the after-effects are not so pronounced.

Acetone and chloroform combine to form **chloretone**, $(\text{CH}_3)_2 \cdot \text{C}(\text{OH}) \cdot \text{CCl}_3$, used extensively as a hypnotic, anodyne, and preservative. Chloroform reacts with concentrated nitric acid to form **chloropicrin**, or nitrochloroform, a lachrymator ("tear gas"):



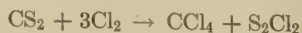
When prepared on a large scale, the chloropicrin is made by the action of bleaching powder on picric acid. It is now used as a fumigant.

Chloroform is sometimes used as a preservative for the prevention of bacterial growth, though for most purposes toluene has largely taken its place. Chloroform is an excellent solvent for many organic compounds; it dissolves fats, rubber, etc.

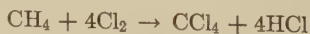
Bromoform, CHBr_3 , is prepared similarly to chloroform. Its anesthetic properties are less marked.

Iodoform (triiodomethane), CHI_3 , is prepared by adding iodine to a warm solution of sodium carbonate containing alcohol or acetone—a method analogous to that for preparing chloroform. The odor of iodoform is both characteristic and powerful; hence the reaction is used as a test for alcohol, acetone, or compounds with similar structural features. Iodoform is a powerful antiseptic and disinfectant, the antiseptic properties being due to its gradual decomposition with the liberation of iodine.

Tetrahalogen Derivatives of the Paraffins, CF_4 , CCl_4 , CBr_4 , and CI_4 . Of these, only the second, **carbon tetrachloride**, is important. It is made commercially by passing chlorine into carbon disulfide, using iron, iodine, or antimony pentasulfide as a catalyst:



We have already mentioned the production of CCl_4 from methane by the action of chlorine:



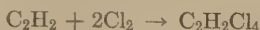
Carbon tetrachloride is a colorless liquid with an ethereal odor. It is a good solvent for resins and is also a constituent of many dry-cleaning

mixtures. It is an anesthetic, but it is not used for this purpose because of its bad effect on the heart. It is used in fire extinguishers ("Pyrene"). Its vapor produces severe headaches. It is also used as a vermifuge in the treatment of hookworm.

Dichlorodifluoromethane, CCl_2F_2 , "Freon-12," is now used as a refrigerant and as a solvent for insecticides.

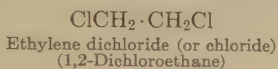
Fluorides are generally made by treating other halides with metallic fluorides such as SbF_3 .

A number of chlorinated paraffins, used as solvents, have been prepared on a commercial scale. One such is tetrachloroethane, made by the action of chlorine on acetylene:

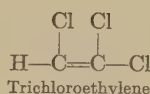
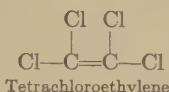
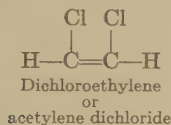


Hexachloroethane, $\text{CCl}_3 \cdot \text{CCl}_3$, is used in the manufacture of fireworks and, when mixed with zinc, for the production of smoke screens.

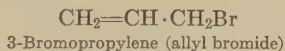
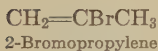
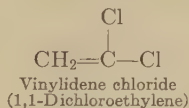
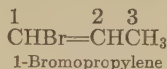
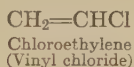
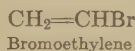
Still others with commercial possibilities are



Halogen Derivatives of Unsaturated Hydrocarbons. The names and structures of a few of these will be given:

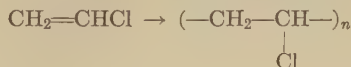


These are used as solvents. Trichloroethylene is also employed as an anesthetic.



($\text{CH}_2=\text{CH} \cdot \text{CH}_2$ is known as the allyl group.)

Chloroprene (p. 43) is an important halogenated unsaturated hydrocarbon. Vinyl chloride and vinylidene chloride polymerize to resins:

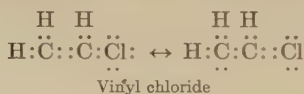


The polyvinyl chloride is used commercially under several names ("Vinylite," "Koroseal," etc.). A copolymer of vinyl chloride and vinyl acetate forms a useful fiber ("Vinyon"); polyvinylidene chloride,

$$\begin{array}{c} \text{Cl} \\ | \\ (-\text{CH}_2-\text{C}-)_n \\ | \\ \text{Cl} \end{array}$$

is made into tubing ("Saran") which serves as a substitute for rubber tubing.

Resonance. Vinyl chloride presents an interesting example of the influence of structure on reactivity. In this compound, chlorine hardly reacts at all; it remains attached firmly to the carbon. The same is true of all unsaturated halides in which the halogen is linked to an olefinic carbon. This unusual stability can be explained by the assumed existence of two possible forms of the molecule which differ only in the arrangement of the valence electrons, and consequently are equally stable; there is "resonance" between the two structures.



Such a substance as vinyl chloride is said to exist as a *resonating system* of the possible structures, rather than definitely as one or another. The possibility of several electronic arrangements for the same atomic layout is connected with increased stability. In these resonating systems, the interatomic (internuclear) distances are found to be less than the corresponding distances in non-resonating molecules.

QUESTIONS

- Write structural formulas for the following compounds: (a) isopropyl chloride; (b) *n*-propyl bromide; (c) isobutyl iodide; (d) 2-bromobutane; (e) methylene fluoride; (f) 1-methyl-2-chlorobutane; (g) ethylene iodide; (h) ethylidene bromide; (i) chloroform; (j) *tert*-butyl bromide; (k) propylene chloride; (l) vinyl bromide; (m) monochloroethylene; (n) trichloroethylene; (o) acetylene dichloride; (p) *sym*-dichloroethylene; (q) acetylene tetrabromide; (r) 2-bromopropene; (s) 4-chloro-2-pentene.
- Give two names for each of the following:

- $$\begin{array}{c} \text{I} & \text{I} \\ | & | \\ \text{(a) } \text{H}:\ddot{\text{C}}::\ddot{\text{C}}:\text{H}; & \text{(b) } \text{H}_2\text{C}=\text{CCl}\cdot\text{CH}_3; & \text{(c) } \text{H}_2\text{C}=\text{CHBr}; & \text{(d) } \text{H}_2\text{C}=\text{CH}\cdot\text{CH}_2\text{Br}; \\ \text{(e) } (\text{CH}_3)_3\text{C}\cdot\text{C}(\text{CH}_3)_3. \end{array}$$

3. Write equations for the preparation of the following compounds:

- | | |
|--------------------------|---------------------|
| (a) ethyl bromide | from ethyl alcohol |
| (b) ethylene bromide | " ethyl alcohol |
| (c) ethylidene bromide | " ethyl alcohol |
| (d) carbon tetrachloride | " carbon disulfide |
| (e) ethylidene bromide | " acetylene |
| (f) vinyl chloride | " acetylene |
| (g) isopropyl chloride | " isopropyl alcohol |
| (h) chloropicrin | " chloroform |

4. Write equations for the reactions of isopropyl bromide with sodium, magnesium, alcoholic alkali, aqueous alkali, KCN, and NH_3 .

5. Write structures for the possible resonance forms of vinyl chloride and of carbonate ion.

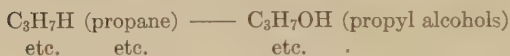
CHAPTER V

ALCOHOLS

Methanol, which is methyl (or wood) alcohol, and ethanol or ethyl (or grain) alcohol, are the two most important substances belonging to this group.

The alcohols may be considered hydrocarbons in which one or more of the hydrogens are replaced by OH groups. They may also be regarded as water in which one of the hydrogens is replaced by R; $\text{H—OH} \rightarrow \text{R—OH}$.

The relationship of the hydrocarbons to the alcohols is shown here:

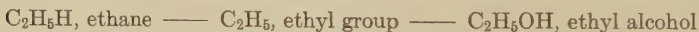


Nomenclature of Alcohols. Several systems are employed.

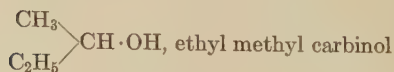
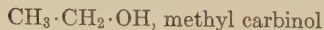
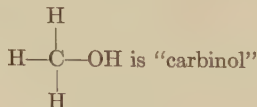
1. In the Geneva system the ending *-e* of the hydrocarbon containing the same number and arrangement of carbon atoms is changed to the ending *-ol*:



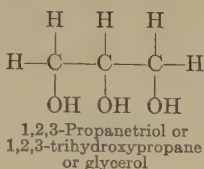
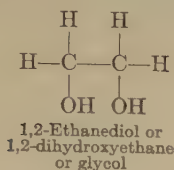
2. The alcohol is named according to the alkyl group it contains:



3. The alcohols are looked upon as “carbinol” derivatives:



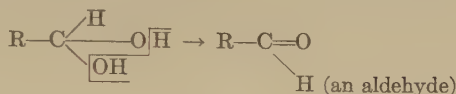
Alcohols may contain more than one OH group provided that they are attached to different carbon atoms; e.g.,



etc.

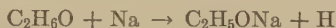
We shall see in a later chapter that the sugars contain several OH groups.

Two or more OH groups attached to the same carbon atom give rise, as a rule, to unstable compounds,

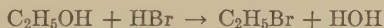


the unstable dihydroxy compound being converted into an aldehyde (or ketone). We shall explain the oxidation of an alcohol to an aldehyde in this manner.

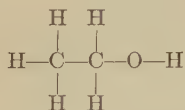
If we take an alcohol, such as ethyl alcohol, $\text{C}_2\text{H}_6\text{O}$, and treat it with sodium, only one atom of hydrogen (out of the six present) is liberated:



This particular atom of hydrogen obviously differs in some way from the other five atoms. The possibility that this difference is due to a difference in position within the molecule is borne out by the fact that, when we treat the alcohol with, say, hydrogen bromide, one atom of bromine replaces one atom of hydrogen and one atom of oxygen—one bromine, in other words, replaces one hydroxyl group:



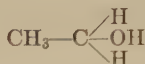
It would seem, therefore, as if one hydrogen in ethyl alcohol is attached, not to the carbon atoms (like the other five hydrogen atoms), but to the oxygen atom:



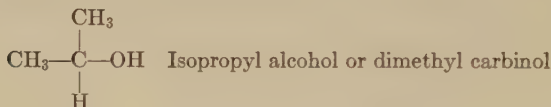
and all the reactions of the many alcohols known (some of which will be discussed presently) strengthen this view.

Types of Alcohols. 1. The presence of the group $\begin{array}{c} \text{H} \\ | \\ -\text{C}-\text{OH} \\ | \\ \text{H} \end{array}$ indicates

a **primary alcohol**: e.g.,



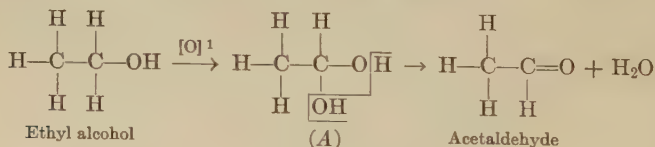
2. The group $\begin{array}{c} | \\ -\text{C}-\text{OH} \\ | \\ \text{H} \end{array}$ indicates a **secondary alcohol**: e.g.,



3. The group $\begin{array}{c} | \\ -\text{C}-\text{OH} \\ | \end{array}$ indicates a **tertiary alcohol**: e.g.,



These three types of alcohols yield various oxidation products. When a primary alcohol is oxidized, we first get an aldehyde; e.g.,



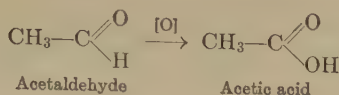
It is assumed that (A) is an intermediate compound, though it has not, as yet, been isolated. It has already been pointed out that a compound containing two OH groups attached to the same carbon atom is usually unstable, water splitting off in the manner shown.

¹ In the laboratory the oxidizing agent used may be aqueous KMnO_4 or $\text{K}_2\text{Cr}_2\text{O}_7$ (in acid solution) or dilute HNO_3 ; industrially, oxidations are often carried out in the vapor phase with air in the presence of catalysts, such as Ag or Cu.

The oxidation of alcohols to aldehydes is a dehydrogenation—a removal of hydrogen—and may actually be performed in the absence of air (or oxygen) by the use of a substance which can remove hydrogen: Pt, Ni, etc.

This conception of oxidation via dehydrogenation has also its application in biochemistry (biological oxidations).

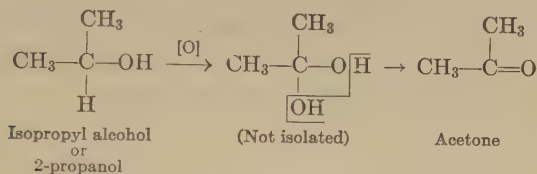
The aldehyde on further oxidation yields the corresponding acid:



It should be observed at this point that the group $-\text{C} \begin{array}{l} \nearrow \text{O} \\ \searrow \text{H} \end{array}$ is characteristic of aldehydes, and the group $-\text{C} \begin{array}{l} \nearrow \text{O} \\ \searrow \text{OH} \end{array}$ is commonly characteristic of organic acids.

We see then that the oxidation of a primary alcohol yields first an aldehyde and then an acid containing the same number of carbon atoms as the original alcohol.

When a secondary alcohol is oxidized we get a ketone; e.g.,



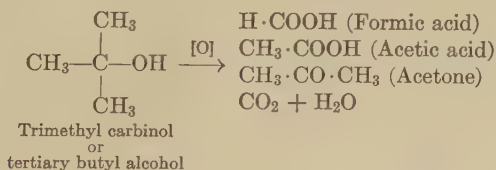
$\text{R} \begin{array}{l} \nearrow \\ \searrow \end{array} \text{C}=\text{O}$ represents ketones, and acetone is the simplest member of the series. On further oxidation we get acids containing fewer carbon atoms than the original ketone or alcohol.

There are two isomeric propyl alcohols, the normal, $\text{CH}_3 \cdot \text{CH}_2 \cdot$

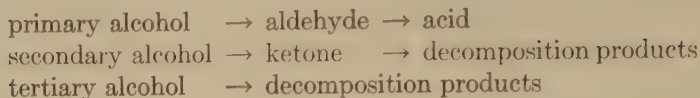
CH_2OH (1-propanol), and the iso, $\text{CH}_3-\text{C} \begin{array}{l} \nearrow \text{H} \\ \searrow \text{OH} \\ | \\ \text{CH}_3 \end{array}$ (2-propanol). The

latter, being a secondary alcohol, yields a ketone—acetone—on oxidation; the normal, being a primary alcohol, yields first an aldehyde—propionaldehyde—and then an acid—propionic acid.

When a tertiary alcohol is oxidized, a mixture of acids and ketones is obtained, each substance formed having fewer carbon atoms in its molecule than the original tertiary compound: e.g.,

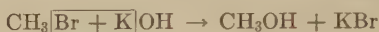
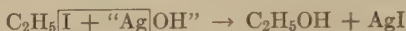


We therefore see that on oxidation

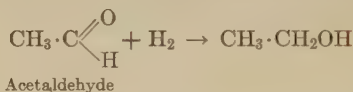


Methods of Preparation. Some alcohols are produced in the course of destructive distillation and fermentation. Among other methods are the following:

1. The action of moist silver oxide or aqueous NaOH or KOH solution on an alkyl halogen compound,

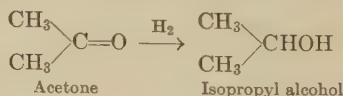


2. The reduction of aldehydes (yielding primary alcohols),

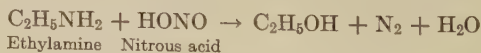


The student will recall that the oxidation of a primary alcohol yields an aldehyde; we may therefore expect that the reduction of the aldehyde will yield the alcohol. The reducing agent may be sodium amalgam and water, or hydrogen in the presence of nickel, etc.

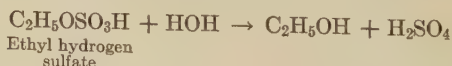
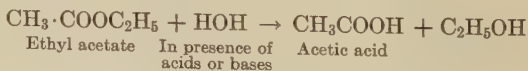
3. The reduction of ketones (yielding secondary alcohols),



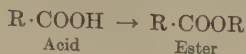
4. The action of nitrous acid on a primary amine (that is, a substance formed when one of the hydrogens in NH_3 is replaced by R, giving $\text{R} \cdot \text{NH}_2$; see p. 159),



5. The hydrolysis of esters,



An ester is an acid in which the ionizable hydrogen is replaced by an alkyl group:



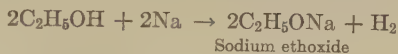
6. Alcohols can be prepared by means of the *Grignard* reaction (p. 87).

Physical Properties. The monohydric alcohols are colorless substances. The compounds from CH_3OH to $\text{C}_4\text{H}_9\text{OH}$ are limpid liquids; those from C_5 to C_{11} are of oily consistency; and those from C_{12} up are solids. The solubility in water decreases with increase in molecular weight. An increase in the number of OH groups in a compound tends to increase the sweetness; e.g., methanol, CH_3OH , is not sweet; glycol, $\text{C}_2\text{H}_4(\text{OH})_2$, is somewhat sweet; glycerol, $\text{C}_3\text{H}_5(\text{OH})_3$, is sweet; and mannitol, $\text{C}_6\text{H}_8(\text{OH})_6$, is still sweeter. The lower alcohols have characteristic odors; the C_8 – C_{12} have rose- or lily-like odors and are used in perfumery; the higher ones are practically odorless.

Chemical Properties. The alcohols, like water (which they resemble in many ways), are neither acid nor alkaline in reaction. Like water, again, the alcohols combine with compounds to form crystalline products; for example,



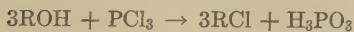
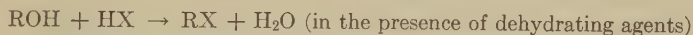
These compounds are said to contain "alcohol of crystallization." Sodium reacts with alcohol as it does with water, only less violently; e.g.,



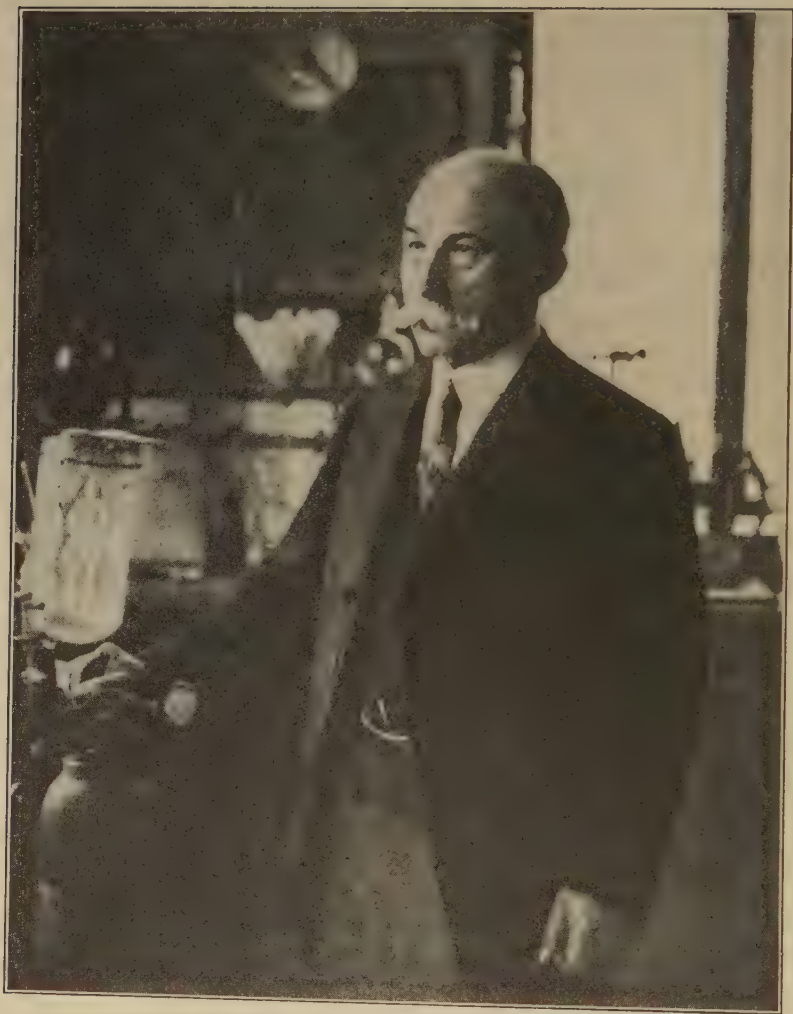
In the scale of relative acidity, alcohols are weaker than water.

As we have seen, the primary alcohols, on oxidation, yield aldehydes and acids; the secondary alcohols, ketones; and the tertiary alcohols, various decomposition products.

The OH group in the alcohol can be replaced by a halogen in a number of ways:



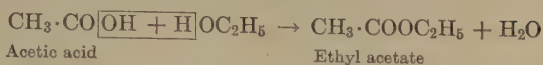
Tertiary alcohols react most readily (even in the cold with HCl), and primary alcohols least.



VICTOR GRIGNARD (1871-1935)

Professor of chemistry at the University of Lyon (France). His discovery of the organo-magnesium compounds and their reactions, for which he received the Nobel prize, has been of inestimable value in the synthesis of many organic compounds.

Alcohols combine with acids to form esters: e.g.,



MONOHYDRIC ALCOHOLS

<i>Alcohol</i>	<i>Formula</i>
Methyl	CH_3OH
Ethyl	$\text{CH}_3 \cdot \text{CH}_2\text{OH}$
<i>n</i> -Propyl	$\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_2\text{OH}$
Isopropyl	$\text{CH}_3 \cdot \text{CH}(\text{OH}) \cdot \text{CH}_3$
<i>n</i> -Butyl	$\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2\text{OH}$
Secondary butyl	$\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}(\text{OH}) \cdot \text{CH}_3$
Isobutyl	$\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \text{CH} \cdot \text{CH}_2\text{OH} \end{array}$
Trimethyl carbinol (tertiary butyl)	$\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \text{CH}_3 \diagup \text{C}(\text{OH}) \\ \diagup \\ \text{CH}_3 \end{array}$
.	.
.	.
Cetyl	$\text{C}_{16}\text{H}_{33}\text{OH}$
Myricyl	$\text{C}_{30}\text{H}_{61}\text{OH}$

Methanol,¹ CH_3OH (also called methyl alcohol, wood alcohol, carbinol, Columbian spirit, and wood spirit). This alcohol does not occur free in nature. It is now manufactured mainly by a catalytic synthesis from the water-gas mixture of carbon monoxide and hydrogen:



The catalyst consists of zinc chromite; the temperature is about 400° ; and the pressure, 200 atmospheres. By changing the catalyst, higher alcohols may be obtained.

Another process utilizes the by-products of the butanol-acetone fermentation. In this fermentation, pure hydrogen and carbon dioxide are generated. An adjustment is made in the relation of hydrogen to carbon dioxide by a simple scrubbing process under pressure, after which the mixture is further compressed and passed over the methanol catalyst at elevated temperatures.

Before the development of its synthesis, methanol was obtained commercially by the destructive distillation of hard wood (maple, beech, birch, oak, etc.). When wood is heated in retorts to about 400° , we obtain gases (used as fuel under the retorts), an aqueous distillate

¹ The name "methanol" is now being generally employed, largely with a view to preventing the use of the substance in the place of grain alcohol.

(known as "pyroligneous acid"), wood tar, and charcoal (which remains in the retorts). The wood tar is a source of antiseptics (wood creosote), disinfectants, fuel, road materials, etc. The pyroligneous acid contains acetic acid as well as methanol and acetone. Wood distillation is now a relatively unimportant source of these materials.

Properties and Uses. Methanol is a colorless liquid with a rather objectionable odor (b.p. 64.7°). It is a poison and gives rise to blindness when taken internally or applied externally. It burns with a blue flame, quite devoid of soot, to CO_2 and H_2O . On oxidation it first forms the corresponding aldehyde, formaldehyde ($\text{H}\cdot\text{CHO}$), and then formic acid ($\text{H}\cdot\text{COOH}$). The alcohol is used very largely as a solvent in the manufacture of varnishes and lacquers, especially those containing shellac; as a solvent for moving-picture films; in the preparation of denatured alcohol; in the manufacture of formaldehyde; in the preparation of various dye intermediates;¹ as an anti-freeze in automobile cooling systems; etc.

Ethyl Alcohol, $\text{C}_2\text{H}_5\text{OH}$ (also called alcohol, ethanol, grain alcohol, Cologne spirit, and wine spirit). The commercial method of preparation is a process called **fermentation** (fermentation is a decomposition brought about by substances [enzymes] secreted by various forms of vegetable and animal life). With the exception of the quantity produced synthetically, ethyl alcohol is obtained by the fermentation of sugar solution and saccharified mashes of starch-containing materials. (The raw material varies in different countries. Sugar and cane molasses from sugar mills and corn are used in the United States; potatoes, in Germany; and beet sugar, in France.)

Molasses, since its sugar content can be easily and economically converted into alcohol, is the raw material for more than 75 per cent of all the ethyl alcohol produced in this country. Blackstrap molasses, containing between 50 and 60 per cent of sugar by weight, a by-product of cane sugar mill operations, is principally used.

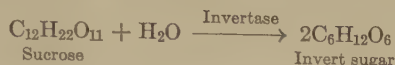
Several sugars are present in blackstrap molasses. Generally the greatest percentage is sucrose, $\text{C}_{12}\text{H}_{22}\text{O}_{11}$. Sugars having the chemical formula $\text{C}_6\text{H}_{12}\text{O}_6$ are also present.

Alcohol is produced from molasses by a fermentation in which the sugars are converted into alcohol by the action of yeast enzymes. The molasses is made up into a mash by mixing with a calculated amount of water, so that the final sugar concentration falls within the range of 15 to 25 per cent by weight. Yeast is prepared in special equipment to insure a pure, vigorous culture and is added to the mash in quantities ranging from 3 to 10 per cent by volume. The acidity of the mash is

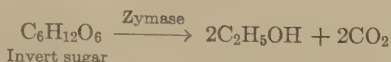
¹ A dye intermediate is an organic compound used in the manufacture of dyestuffs.

regulated carefully to control the action of impurities in the mash upon the yeast and yet permit rapid conversion of the sugars to alcohol.

The yeast has a double action upon the sugar. This is brought about by the presence in the yeast of two enzymes, invertase and zymase. In the presence of invertase, sucrose undergoes conversion to invert sugar (glucose and fructose):



The invert sugar is then converted by the enzyme zymase into ethyl alcohol and carbon dioxide:



During the fermentation the temperature is very carefully regulated. At times, depending on the particular characteristics of the molasses used, it is necessary to add a small amount of nutrients to the mash to sustain the activity of the yeast. The time required to convert the sugars to alcohol, with maximum yields, varies between 36 and 48 hours. It might be noted here that the yeast itself does not undergo change during the process but merely acts as the agency for conversion of sugar to alcohol.

The resulting mash, at the completion of fermentation, contains from 6 to 12 per cent of alcohol and is called "beer."

The beer is passed into a continuous distilling unit, and the alcohol is separated from the residue, called slop, by distillation with steam. Although alcohol is the main product of yeast activity, small quantities of other substances are produced, such as aldehydes, esters, and fusel oil, which distil over with the alcohol. These substances do not decrease the solvent powers of the alcohol but they impart a distinct odor which is undesirable. Also, they have value as by-products in their purified form. It is, therefore, necessary to rectify the crude alcohol by redistillation. This method of purification has been developed to a high degree, and alcohol (before denaturation) is one of the purest chemicals.

Among the by-products recovered from the distillation process are carbon dioxide (compressed either to a liquid or a solid), potash for the manufacture of fertilizers, vitamin concentrates for feedstuffs, and binders for the foundry and coal-processing industries.¹

The use of starch, in the form of grain, as a raw material for alcohol fermentation dates back to very ancient times. Among the relics found

¹ Much of this information was obtained from a pamphlet published by the U. S. Industrial Alcohol Corp.

in the old tombs of Egypt have been vessels containing residues which show starch grains and yeast and indicate that the art of distilling was practiced in the days of the Pharaohs.

Starch is not directly fermentable by yeast and must, therefore, be converted to sugar. The procedure is to cook the starch (grain), cool, and then treat with barley malt, whose enzymes convert substantially all the starch to sugar.

In fermentation the most outstanding difficulty to contend with is infection. Its control, for the most part, rests on a single factor in the solution, namely, the acidity. If the *pH* is kept down to 5 or preferably a little below, most of the infecting organisms are held back in their growth, and the resulting fermentation is essentially a pure culture yeast fermentation. Lactic acid is commonly used for this purpose.

Such substances as grape juice, corn syrup, and molasses are already rich in glucose. Here the preliminary diastase treatment to convert starch into glucose is unnecessary.

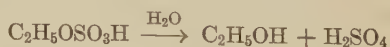
It is of interest to note that phosphates are necessary for alcoholic fermentation. Compounds of glucose and phosphoric acid, and even other compounds of phosphorus, have been isolated from fermentation batches.

Commercial ethyl alcohol contains 96 per cent of alcohol by volume, which is the composition of a constant-boiling-point (azeotropic) mixture of alcohol and water (78.15°); in other words, distillation will not yield a more concentrated aqueous alcohol.

"Absolute" or practically anhydrous ethanol can be obtained by the addition of calcium oxide (quicklime) or anhydrous copper sulfate (which act as dehydrating agents) to the liquid, allowing to stand a day or two, and then distilling the mixture.

A more practical industrial method for obtaining absolute alcohol consists of adding benzene to 96 per cent alcohol; distillation yields first a ternary mixture of benzene, water, and alcohol with a constant boiling point (64.85°) lower than that of the 96 per cent solution; thus the water is removed. The benzene is removed in the form of a binary mixture with alcohol (b.p. 68.25°).

A process for the manufacture of synthetic ethyl alcohol utilizes ethylene from natural gas and cracking gases, and is therefore assuming great importance:



Properties and Uses. Ethyl alcohol is a colorless liquid having a characteristic odor and a sharp burning taste (b.p. 78.3°). In the form

of tinctures (alcoholic solutions or extracts of medicinal substances) it is extensively used in medicine.

The use of alcohol in industry is very extensive. As a preservative, as an antiseptic, in the preparation of denatured alcohol and various drugs and medicinals, as a solvent, as an "anti-freeze," as an essential constituent in the manufacture of iodoform, chloroform, vinegar, and ether, alcohol is in constant demand. Additional uses are summarized in the following chart (p. 70). Avertin, a widely used anesthetic, is tribromoethanol, $\text{CBr}_3 \cdot \text{CH}_2\text{OH}$.

During World War II the alcohol needs in the munitions and synthetic-rubber industries became so considerable that little whisky distilling was allowed.

Denatured Alcohol. Denatured alcohol has been made unfit for drinking purposes and external application, but can still be used in industry. Some of the substances used in "denaturing" are methanol, benzene, ether, acetone—substances with disagreeable odors and flavors and possessing poisonous properties. More than sixty different formulas are permitted in the United States for the preparation of denatured alcohol for various industrial uses. Denatured alcohol is tax-free.

Medicated alcohol is alcohol unfit for drinking purposes but suitable for external application. Some of the substances used in the preparation of medicated alcohol are tartar emetic, formaldehyde, phenol, diethyl phthalate, benzene, acetone, and zinc phenosulfonate.

Alcohol in Beverages. Beer = 2–5 per cent; wine = 7–11 per cent; fortified wine = 17–20 per cent; whisky, brandy, gin, rum, etc. = 40–75 per cent.

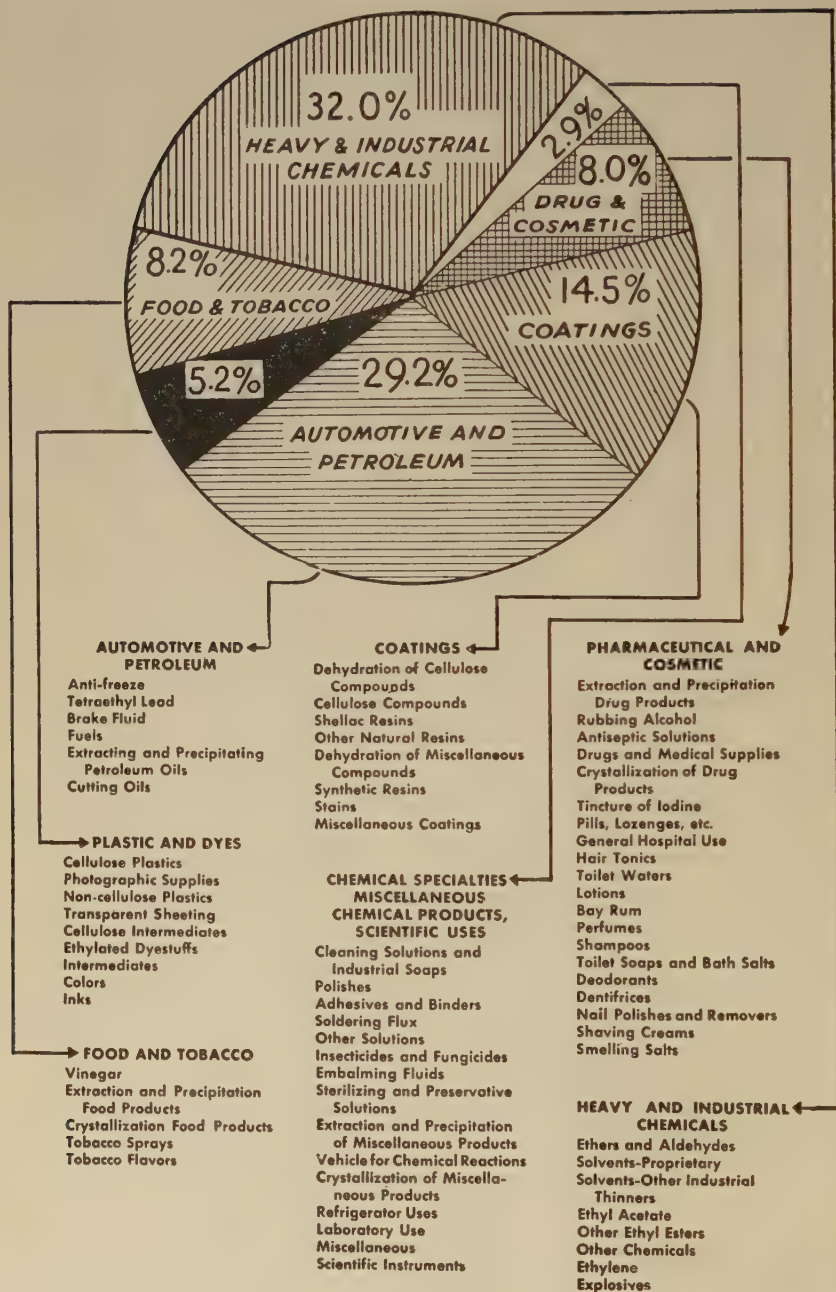
The percentage of alcohol in a number of pharmaceutical preparations is relatively high. Aromatic spirit of ammonia = 62–68 per cent; spirit of camphor = 80–87 per cent; tincture of iodine = 80–85 per cent, etc. For further details consult the *U. S. Pharmacopæia*.

"Alcohol proof" expresses the strength of alcohol; it represents the percentage of alcohol by volume multiplied by 2. For example, 190 proof alcohol represents 95 per cent by volume.

Whenever fermented liquors are distilled, we get not only ethyl alcohol but also small quantities of esters and a number of the higher alcohols, the mixture of these higher alcohols being known as **fusel oil**. Some claim that the presence of fusel oil in liquors is far more harmful than the ethyl alcohol itself. In this connection the following information may be of interest. We know that the principal component of

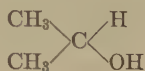
fusel oil is **isoamyl alcohol**, $\begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} \text{CH} \cdot \text{CH}_2 \cdot \text{CH}_2\text{OH}$, and we know that

INDUSTRIAL USES OF ALCOHOL

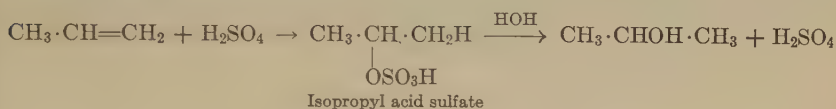


the source of this is isoleucine, an amino acid obtained from the protein present in cereal or potato. The bacteria present convert the isoleucine into isoamyl alcohol. It has, however, been shown that this conversion—and hence the production of isoamyl alcohol—may be prevented by the addition of ammonium salts, which the bacteria prefer.

Isopropyl alcohol, isopropanol, 2-propanol,



can be made by the reduction of acetone. It is now made by passing propylene gas into sulfuric acid and hydrolyzing the product.



This alcohol is used as a substitute for ethanol in shampoos, lotions, etc.

n-Butyl alcohol, 1-butanol, $\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{OH}$, is produced by the action of the bacterium *Clostridium acetobutylicum* on materials containing starches and carbohydrates (corn) (*Weizmann* process) and is used on a large scale in the nitrocellulose lacquer industry as a solvent for shellac and for the preparation of esters. In the *Weizmann* fermentation, the organic liquids produced include *n*-butyl alcohol, acetone, and ethyl alcohol in the ratio of 6 : 3 : 1. The gases evolved during the fermentation are CO_2 and H_2 .

Amyl alcohols are at present manufactured on a commercial scale from the pentane fraction of natural gas by the following series of reactions. The mixture is a useful solvent.



Isoamyl alcohol, $\text{C}_5\text{H}_{11}\text{OH}$, is converted to isoamyl acetate and thus used in the manufacture of varnishes and fruit essences.

A number of the higher alcohols are used for the preparation of esters, ethers, amines, etc. Examples of these are *n*-hexanol, $\text{CH}_3(\text{CH}_2)_4 \cdot \text{CH}_2\text{OH}$; methyl amyl carbinol, $\text{CH}_3 \cdot (\text{CH}_2)_4 \cdot \text{CHOH} \cdot \text{CH}_3$; "octyl" alcohol, $\text{C}_4\text{H}_9 \cdot \text{CH}(\text{C}_2\text{H}_5) \cdot \text{CH}_2\text{OH}$; etc.

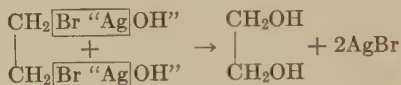
Cetyl alcohol, $\text{C}_{16}\text{H}_{33}\text{OH}$, forms (as palmitic ester) the chief constituent of spermaceti (a waxlike substance found in the head of the sperm whale), while **myricyl alcohol**, $\text{C}_{30}\text{H}_{61}\text{OH}$, is present as palmitic ester in beeswax and in carnauba wax. The alcohols are prepared from all these esters by hydrolysis with boiling alcoholic KOH solution.

High-molecular-weight alcohols are made by catalytic oxidation of paraffins and by catalytic hydrogenation of fats.

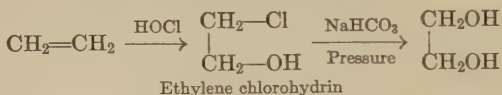
Dihydric Alcohols or Glycols. Alcohols containing two hydroxyl groups are known as glycols. They show marked hygroscopic properties, which are made use of in moistening and softening glue, casein, tobacco, etc. They are soluble in water but, nevertheless, are good solvents for gums, resins, essential oils, etc. The simplest and most important of these glycols is dihydroxyethane, known as **ethylene glycol**, CH_2OH . It is a compound intermediate in composition between ethyl



alcohol and glycerol, and its properties are intermediate between those of the two compounds. It may be prepared by the action of silver oxide on the corresponding dibromo compound:



but commercially it is made from ethylene:

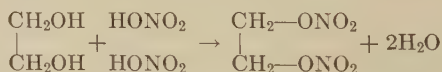


OR



Ethylene glycol is used as a solvent, anti-freeze ("Prestone"), cooling fluid for aviation engines, and preservative. It is a toxic substance. The general chemical properties resemble those of the alcohols, except that here we are dealing with two OH groups instead of one OH group.

Ethylene glycol reacts with HNO_3 (in the presence of H_2SO_4) to produce ethylene dinitrate (glycol dinitrate):



Glycol dinitrate is used in the manufacture of low-freezing dynamite. It is less sensitive to shock than nitroglycerin, though equally sensitive to detonation.

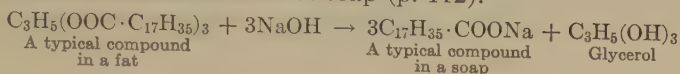
Ethylene chlorohydrin is used for the introduction of the hydroxyethyl group into organic compounds. It has been found effective in forcing the early sprouting of dormant potatoes.

Several other glycols, such as 1,2-propylene glycol, have become available for commercial purposes.

Trihydric Alcohols. The best known of this group is **glycerol** (also called glycerin), CH_2OH (or 1,2,3-propanetriol), which is produced as a



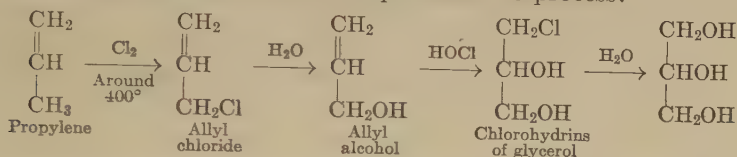
by-product in the manufacture of soap (p. 112).



Details of this process will be given in the chapter on esters (p. 113).

Glycerol is formed in the digestive tract when the fat in food is hydrolyzed by the enzyme lipase of the pancreatic juice.

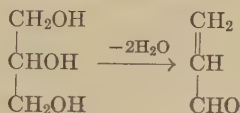
A synthetic method for the production of glycerol has been developed. The following series of reactions represents the process:



Glycerol is also made by "hydrogenolysis" of carbohydrates (splitting of sugars by hydrogen); but the most practical process is still the saponification of fats which, therefore, become strategic materials in time of war.

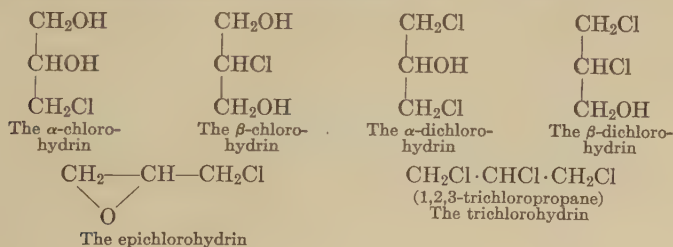
Properties and Uses. Glycerol is a colorless, odorless, syrupy, sweet-tasting liquid. It is miscible with water and alcohol and is a good solvent; it is a dehydrating as well as a moistening agent. It is used in medicine, as a sweetening agent, as a preservative for tobacco, in perfumery, in cosmetics, in ink for rubber stamps, in cellophane, etc.

When glycerol is heated alone or in the presence of a dehydrating agent such as KHSO_4 , **acrolein** is produced:

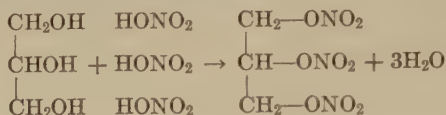


The odor of burnt fat is due to the production of acrolein.

The following chlorohydrins of glycerol are known:



As may be seen from its formula, glycerol is both a primary and a secondary alcohol and may, therefore, be expected to show the properties of both types of alcohols. When glycerol is oxidized, aldehydes, acids, and ketones are formed. Treatment of glycerol with acids gives esters. When nitric acid and glycerol react, one of the compounds obtained is important, namely, the glyceryl trinitrate or, as it is commonly and wrongly called, **nitroglycerin**.



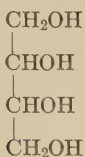
Concentrated sulfuric acid is added to remove the water that is formed. When nitroglycerin explodes, the products formed are CO_2 , H_2O , N_2 , and N_2O .

Nitroglycerin is a dangerous explosive to handle, but, when mixed with an inert substance, like infusorial earth or "kieselguhr," thereby becoming **dynamite**, it can be handled with much less risk. Since kieselguhr is an inert substance and lessens the strength of the nitroglycerin, it is now customary to use an absorbent mixture such as wood pulp (a fuel) and an oxidizing substance, like sodium nitrate, which not only absorbs the nitroglycerin but also adds to the energy produced when the dynamite is exploded.

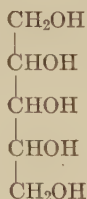
We owe the invention of dynamite to Alfred Nobel, a Swedish engineer, who accumulated a fortune as a result of his invention and who bequeathed it to the Swedish Academy for the purpose of endowing the Nobel prizes.

Vapors of nitroglycerin produce severe headache. In medicine, a 1 per cent solution in alcohol is used as a heart stimulant; it has a powerful action on the arteries.

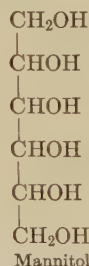
Polyhydric Alcohols. The careful oxidation of the penta- and particularly the hexa-hydroxy alcohols leads to the compounds known as sugars; and, conversely, the reduction of some sugars yields useful polyhydric alcohols.



Erythritol



Arabitol



Mannitol

Erythritol occurs in nature, either in the free or combined state, in algae and certain lichens. A source of arabitol is gum arabic. The source of mannitol was the manna ash tree, which, however, is not believed to be related to the "manna" of the Bible. The hexanitrate of mannitol is a high explosive, used as a primer to initiate explosives. Dulcitol and sorbitol are isomers of mannitol. Most of these alcohols are made by the reduction of the corresponding sugars.

UNSATURATED ALCOHOLS

$\text{CH}_2=\text{CHOH}$, ethenol, vinyl alcohol, is an unstable compound.

$\text{CH}_2=\text{CH}\cdot\text{CH}_2\text{OH}$, allyl alcohol, 2-propen-1-ol, is present in pyro-ligneous acid.

Such compounds possess the general characteristics of alcohols, and, being unsaturated compounds, they form additive products with hydrogen, with halogens, with halogen acids, etc.

QUESTIONS

- Write structural formulas for all the monohydric alcohols from $\text{C}_2\text{H}_5\text{OH}$ to $\text{C}_4\text{H}_9\text{OH}$, inclusive. Name each as a derivative of carbinol.
- Outline a proof for the structure of ethyl alcohol.
- What is meant by (a) a primary alcohol; (b) a secondary alcohol; (c) a tertiary alcohol? Discuss the oxidation products of these three types of alcohols. Write equations for these oxidations.
- Indicate what is meant by the following terms: (a) denatured alcohol; (b) medicated alcohol; (c) absolute alcohol; (d) 190 proof alcohol; (e) fusel oil; (f) pyro-ligneous acid.
- Write structural formulas for: (a) carbinol; (b) methyl carbinol; (c) isobutyl alcohol; (d) 2-propanol; (e) secondary *n*-butyl alcohol; (f) *tert*-butyl alcohol; (g) ethylene glycol; (h) isoamyl alcohol; (i) ethyl isopropyl carbinol; (j) primary isobutyl alcohol.
- Write equations for the preparation of the following compounds.

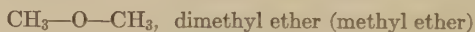
(a) ethyl alcohol	from ethyl iodide
(b) ethyl alcohol	" glucose
(c) methyl alcohol	" carbon monoxide
(d) isopropyl alcohol	" propylene
(e) <i>n</i> -amyl alcohol	" <i>n</i> -pentane
(f) glycol	" ethylene
(g) isobutyl bromide	" isobutyl alcohol
(h) 2-butanol	" 1-butanol
- Write the formulas for the chlorohydrins of glycerol, and name them.
- On treatment with sodium, 4 grams of a pure alcohol yielded 327 ml of hydrogen gas at 22°C and 765 mm. Write all the possible structural formulas of the alcohol.

CHAPTER VI

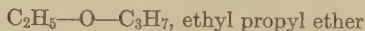
ETHERS

Ethers may be considered as alcohols in which the H of the ROH is replaced by an R group; or they may be looked upon as HOH in which both hydrogens are replaced by R groups. The ethers are really organic oxides. For example, $\text{C}_2\text{H}_5\text{—O—C}_2\text{H}_5 = (\text{C}_2\text{H}_5)_2\text{O} = \text{ethyl oxide}$, commonly known as "ether."

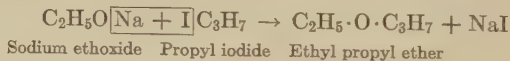
Types of Ethers. If the two R's represent the same groups, then we get a **simple ether**.



If the two R's represent different groups, we get a **mixed ether**.

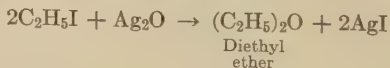


General Methods of Preparation. Most generally applicable is the action of an alkyl halide on a sodium alkoxide; e.g.,



This method, the *Williamson synthesis*, enables one to prepare either a simple or a mixed ether.

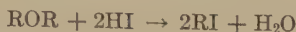
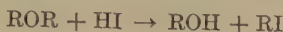
Heating a mixture of silver oxide and alkyl halide, e.g.,



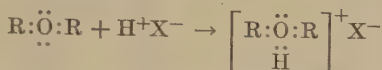
is of little use, except to prove the oxide structure of ethers.

General Properties. The ethers of low molecular weight are colorless, neutral liquids, more volatile than the corresponding alcohols and lighter than water. Being very stable and inactive, they are used as solvents. The ethers, especially the lower members, are highly flammable.

Sodium, ammonia, alkalies, and dilute acids have no action on ethers. Hydrogen iodide (as well as HBr and concentrated H_2SO_4) splits ethers at high temperatures.

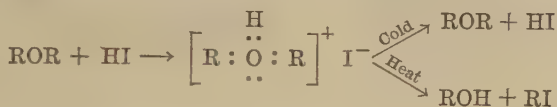


At very low temperatures, however, HI, as well as HCl, HBr, H_2SO_4 , and many other inorganic compounds, forms saltlike complexes with ethers. These are known as **oxonium** compounds and are represented in the same manner as the corresponding ammonium and hydronium structures (p. 14);

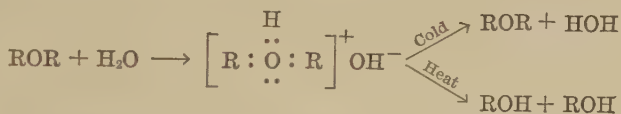


Upon addition of water at room temperature, the original components are regenerated from the addition complex.

At higher temperatures, these oxonium compounds¹ may split in another fashion to give the products indicated previously; e.g.,



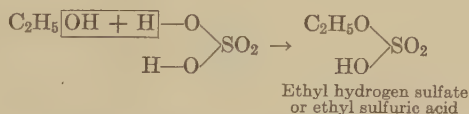
The decomposition of ethers by steam at 150°C may be explained similarly:



Chlorine replaces the hydrogens in the alkyl groups, preferentially on the C atom next to the O.

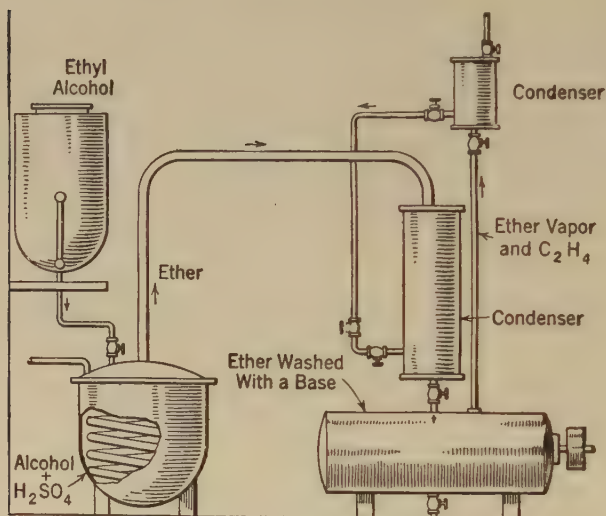
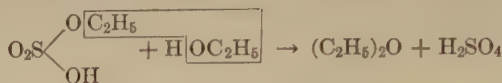
Diethyl ether, $\text{C}_2\text{H}_5\text{—O—C}_2\text{H}_5$ (also known as ether, sulfuric ether, and ethyl oxide), is the most important member of this group.

Ether is manufactured by the "continuous etherification process." Equimolecular proportions of alcohol and sulfuric acid are mixed:



¹ Similar oxonium compounds have been shown to form with alcohols at low temperatures: $\text{ROH} + \text{HX} \rightarrow [\text{ROH} \cdot \text{H}]^+\text{X}^-$. These may be intermediates in the formation of halides.

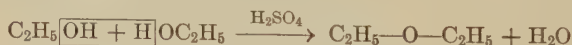
The mixture is now heated to 130–140°, and more alcohol is added:



Manufacture of Ether.

The sulfuric acid is regenerated and used over again until the acid becomes too weak to react with the alcohol.

The equation may be condensed into:



Ether is now also made by the dehydration of two moles of ethyl alcohol, using Al_2O_3 as a catalyst (temperature, 240–260°). Still another method (see chart facing p. 80) employs the following reactions:



Properties. Ethyl ether is a colorless, volatile liquid, with a very characteristic odor (b.p. 34.6°; specific gravity = 0.736 at 0°). It is highly flammable, burning with a luminous flame, and is explosive when mixed with air and ignited. Upon standing, ether combines with oxygen to form peroxides, and these are highly explosive. This tendency to form peroxides may be decreased by the addition of a small amount of water or of a reducing agent (iron wire). Ether is slightly soluble

in water and is used to extract certain substances from aqueous solution. As a solvent for fats, oils, resins, alkaloids, etc., ether is unsurpassed. It can be used as a solvent for quite a number of organic substances. It also dissolves iodine, bromine, sulfur, phosphorus, ferric chloride, etc. It is used with alcohol as a nitrocellulose solvent in the manufacture of guncotton, collodion solutions, and pyroxylin plastics. Because of its rapid evaporation, it can be used for refrigerating purposes. As an anesthetic, it was introduced in surgery both by Dr. Long of Jefferson, Georgia, and by Dr. Morton, a Boston dentist. As an anesthetic, ether is preferred to chloroform, for the physiological effects can be controlled better. Ether for this purpose must be highly purified.

Ether, chloroform, and other anesthetics are, chemically, more or less inert substances and are more soluble in lipids—typical cell constituents—and lipid solvents than in water.

Other Ethers. Many other ethers are now available commercially as a result of the large-scale production of the corresponding alcohols.

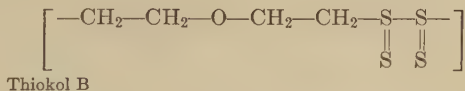
$\text{CH}_3 \cdot \text{O} \cdot \text{CH}_3$, dimethyl ether.

$i\text{-C}_3\text{H}_7 \cdot \text{O} \cdot \text{C}_3\text{H}_7$, diisopropyl ether, is used, among other things, for extracting nicotine from tobacco.

$\begin{array}{c} \text{CH}_2=\text{CH} \\ \text{CH}_2=\text{CH} \end{array} \text{O}$, divinyl ether, an anesthetic.

$\begin{array}{c} \text{CH}_2\text{OC}_2\text{H}_5 \\ | \\ \text{CH}_2\text{OC}_2\text{H}_5 \end{array}$, ethylene glycol diethyl ether, also known as diethyl cellosolve, dissolves both oil and water.

2,2'-Dichlorodiethyl ether, $\text{ClCH}_2 \cdot \text{CH}_2 \cdot \text{O} \cdot \text{CH}_2 \cdot \text{CH}_2\text{Cl}$ ("Chlorex"), containing both the alkyl halide and ether combinations, is an exceptionally good solvent for fats, waxes, etc. It has a high boiling point (178°) and resists hydrolysis. It is used for refining lubricating oils, and in the textile industry to facilitate the action of soap solutions. It condenses with sodium tetrasulfide to form a polymer, **Thiokol**, which is a synthetic rubber:

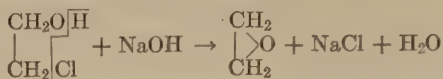


Thiokol B

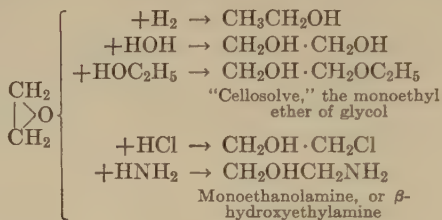
Other dihalides (ethylene dichloride, for example) yield similar products.

Ethylene Oxide, etc. Ethylene oxide, $\begin{array}{c} \text{CH}_2 \\ | \\ \text{—O—} \\ | \\ \text{CH}_2 \end{array}$, may be looked upon as a cyclic or inner ether as well as an anhydride of glycol. It is produced

by distilling ethylene chlorohydrin (made from ethylene) with alkali:

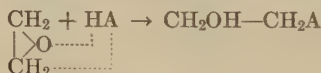


It is a very reactive compound and is used in synthesis. It combines readily with substances with labile hydrogens, for example, water, alcohols, acids, ammonia:



(See chart facing p. 80.)

Other reactions which yield useful products are shown in the chart. Note that all these reactions of ethylene oxide are addition reactions:

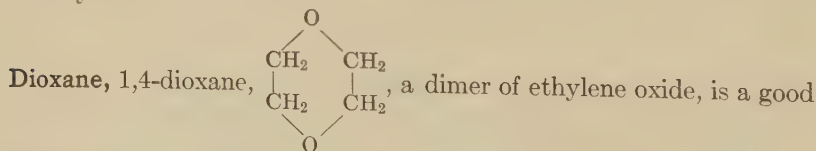


The products contain functional groups in addition to the OH group.¹ Many of these products are ethers and are useful solvents. The "Cellosolves" and "Carbitols" are solvents for various types of coatings. The ethanolamines are used to absorb acid gases (H_2S) and moisture, and to form soaps (with fatty acids) soluble in non-aqueous and aqueous solvents.

Ethylene oxide is a good fumigant and insecticide. "Carboxide," a mixture of carbon dioxide and ethylene oxide, is an effective, harmless fumigant. Propylene oxide, $\text{CH}_3-\text{CH}-\text{CH}_2$, is also available in-



dustrially.



solvent for many organic and inorganic compounds, including water.

¹ The OH group is relatively polar and makes for solubility in water; the ether grouping present in many of these derivatives accounts for solubility in ethers and ether-soluble substances.

NATURAL GAS

$\text{CH}_4, \text{C}_2\text{H}_6, \text{C}_3\text{H}_8, \text{C}_4\text{H}_{10}$

Resins
Polymerization
 $\text{CH}_2=\text{CHCl}$ (1)

NaOH

Cl_2 at 0°

$\text{CH}_2\text{Cl}\cdot\text{CH}_2\text{Cl}$

NaOH (Pressure)

NH_3
 $\text{CH}_2\cdot\text{NH}_2$
 $\text{CH}_2\cdot\text{NH}_2$

NaOH
 $\text{CH}_2\text{OH}\cdot\text{CH}_2\text{OH}$ (4)

NaCN
 $\text{CH}_2\cdot\text{CN}$
 $\text{CH}_2\cdot\text{CN}$

$\text{CH}_2=\text{O}$
 $+\text{CH}_2$

CH_2
 CH_2
 O

HNO_3
(H_2SO_4)
 $\text{CH}_2\cdot\text{ONO}_2$ (5)
 $\text{CH}_2\cdot\text{ONO}_2$ (5)

Hydrolysis
 $\text{CH}_2\cdot\text{COOH}$ (6)
 $\text{CH}_2\cdot\text{COOH}$ (6)

H_2SO_4
 $\text{C}_2\text{H}_5\text{HSO}_4^+(\text{C}_2\text{H}_5)_2\text{SO}_4^-$

H_2O
 $\text{C}_2\text{H}_5\text{OH}$ $\text{C}_2\text{H}_5\cdot\text{O}\cdot\text{C}_2\text{H}_5$

Oxid.
 $\text{CH}_3\cdot\text{CHO}$

alkali
 $\text{CH}_3\cdot\text{CHOH}\cdot\text{CH}_2\cdot\text{CHO}$

+ Dialdol
 $\text{CH}_3\cdot\text{CH}:\text{CH}\cdot\text{CHO}$ (22)

$-\text{H}_2\text{O}$
 $\text{CH}_3\cdot\text{CH}:\text{CH}\cdot\text{CHO}$ (22)

Red.
 $\text{CH}_3\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{OH}$

oxid.
 $\text{CH}_3\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CHO}$

$\text{CH}_2\cdot\text{NH}_2$
 CH_2
 CH_2
 $\text{CH}_2\cdot\text{NH}_2$

$+\text{CH}_2$
 CH_2
 CH_2
 $\text{CH}_2\cdot\text{OH}$

$\text{CH}_2\cdot\text{OH}$
 CH_2
 CH_2
 CH_2
 $\text{CH}_2\cdot\text{OH}$

* Ethyl Ether = Carbitol
* Butyl Ether = Butyl Carbitol

CHEMICAL AND COMMERCIAL

(1) Vinyl Chloride.

(2) Ethylene Chlorohydrin.

(3) Ethylene Oxide.

(4) Ethylene Glycol.

(5) Ethylene Dinitrate - Glycol Dinitrate.

(6) Succinic Acid.

(7) Triethanolamine.

(8) Diethanolamine.

(9) Monoethanolamine.

(10) Ethyl Ether of Ethylene Glycol - Cellulosolve.

(11) Methyl Cellulosolve.

(12) Butyl Cellulosolve.

(13) 1,4 - Dioxane.

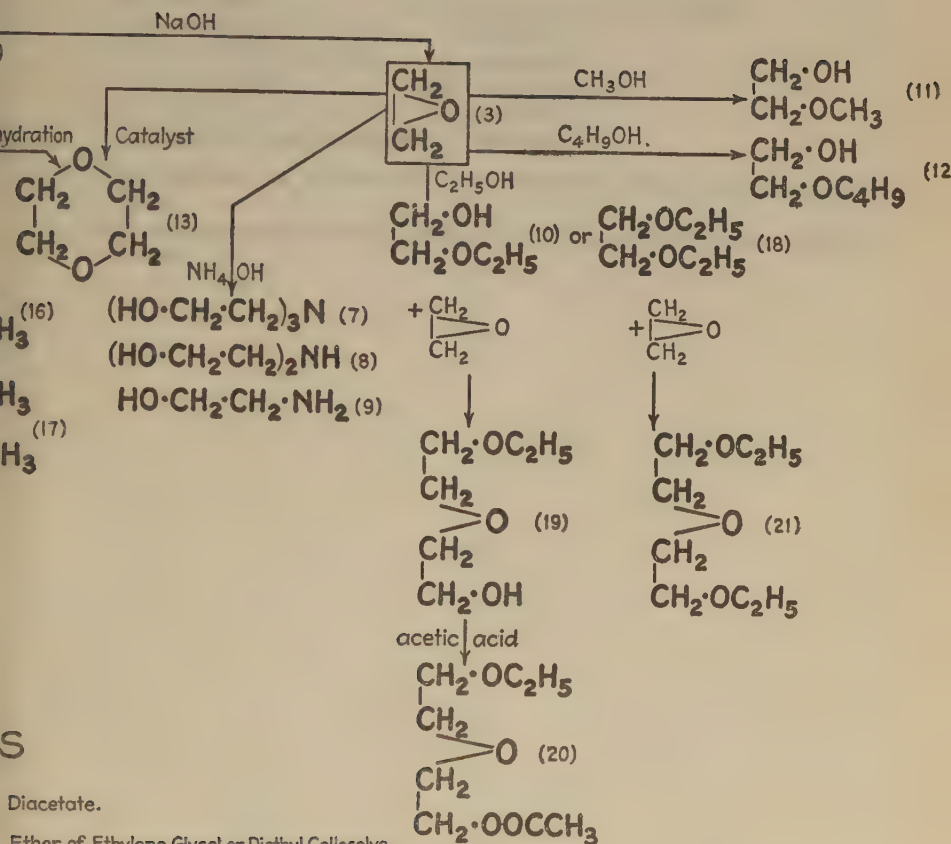
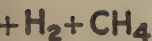
(14) Diethylene Glycol.

(15) Triethylene Glycol.

(16) Glycol Monoacetate.

normal, iso.), C_5H_{12}

→ Cracked to C_2H_4 , C_3H_6 , etc.



S

Diacetate.

Ether of Ethylene Glycol or Diethyl Cellosolve.

hyl Ether of Diethylene Glycol or Carbitol

ol Acetate.

Ether of Diethylene Glycol or Diethyl Carbitol.

aldehyde.

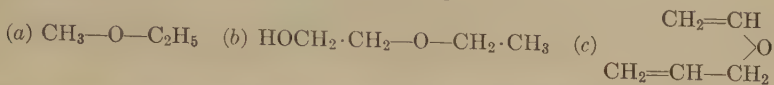
Dichloroethyl Ether.

Diaminoethyl Ether.

QUESTIONS

1. Methyl ether and ethyl alcohol are isomers. What chemical tests could be used to differentiate between the two?

2. Give two names for each of the following compounds:



3. What types of compounds are formed when ethers are allowed to stand? What danger is involved in heating ethers containing such compounds?

4. Write equations for the preparation of the following compounds:

(a) diethyl ether	from ethyl alcohol (two methods)
(b) diethyl ether	" ethylene
(c) methyl isopropyl ether	" propylene
(d) <i>n</i> -butyl alcohol	" <i>n</i> -butyl ether
(e) propylene oxide	" propylene
(f) 1-hydroxy-2-ethoxyethane	" ethylene

5. Write equations for all reactions possible between ethanol and concentrated H_2SO_4 .

6. How may we account for the fact that Cellosolves and Carbitols are such good solvents?

CHAPTER VII

ALDEHYDES AND KETONES

An aldehyde, $R \cdot CHO$, may be regarded as a hydrocarbon in which a hydrogen atom has been replaced by the $\cdot CHO$ group. The type formula for an aldehyde is $R-C \begin{array}{l} \nearrow O \\ \searrow H \end{array}$, and for a ketone, $\begin{array}{l} R \\ R \end{array} > C=O$.

Since both have the $>C=O$ or *carbonyl* grouping as well as a number of common properties, they will be considered in the same chapter. The double bond of the carbonyl group indicates reactivity.

(In the chapter on sugars, the student will discover that most of the sugars contain either aldehyde or ketone groupings, and that a number of their properties depend upon these groups; therefore, much that is gleaned from this chapter can be applied later.)

Nomenclature of Aldehydes. 1. Change the *-e* ending of the hydrocarbon having the same number of carbon atoms (or the *-ol* ending of the alcohol) to *-al* (Geneva system).

C_2H_6 , ethane — C_2H_5OH , ethanol — $CH_3 \cdot CHO$, ethanal

2. The aldehydes may also be named after the acids formed when the aldehydes are oxidized.

$H \cdot COOH$, formic acid — $H \cdot CHO$, formic aldehyde or formaldehyde

$CH_3 \cdot COOH$, acetic acid — $CH_3 \cdot CHO$, acetic aldehyde or acetaldehyde

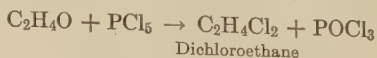
$C_2H_5 \cdot COOH$, propionic acid — $C_2H_5 \cdot CHO$, propionic aldehyde or propionaldehyde

$C_3H_7 \cdot COOH$, butyric acid — $C_3H_7 \cdot CHO$, butyric aldehyde or butyraldehyde
etc.

$R \cdot COOH$ — $R \cdot CHO$

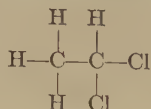
Never write $\cdot C-OH$ to represent the aldehyde grouping, but always $\cdot CHO$. Remember that OH stands for hydroxyl; in alcohols the linking is $R-O-H$, and in aldehydes $R-C \begin{array}{l} \nearrow O \\ \searrow H \end{array}$.

When an aldehyde is treated with phosphorus pentachloride, the reaction is quite different from that obtained when PCl_5 acts on an alcohol. Taking acetaldehyde as an example,

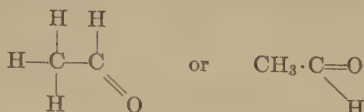


Dichloroethane

An examination of the dichloroethane reveals that it is the unsymmetrical variety, the two chlorine atoms being attached to the same carbon atom,



which suggests that the oxygen atom in aldehyde occupies a position in the chain corresponding to these two chlorine atoms; that is,



Nomenclature of Ketones. 1. Change the *-e* ending of the hydrocarbon with the same number of carbon atoms to *-one* (Geneva system):

C_3H_8 , propane — $\text{CH}_3 \cdot \text{CO} \cdot \text{CH}_3$, propanone, commonly known as acetone

C_4H_{10} , butane — $\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CO} \cdot \text{CH}_3$, butanone

C_5H_{12} , pentane — $\text{CH}_3 \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_3$, 2-pentanone
 $\text{CH}_3\text{CH}_2\text{COCH}_2\text{CH}_3$, 3-pentanone

etc.

The type structure for ketones, $\text{R} \cdot \text{CO} \cdot \text{R}$, indicates that the simplest ketone must contain at least three carbon atoms.

2. Name the compound in accordance with the groups represented by R, remembering that >C=O is the ketonic grouping:

$\text{CH}_3 - \text{CO} - \text{CH}_3$, dimethyl ketone

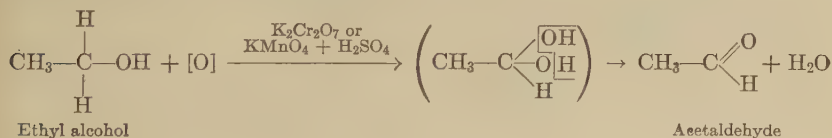
$\text{C}_2\text{H}_5 - \text{CO} - \text{CH}_3$, ethyl methyl ketone

$\text{C}_2\text{H}_5 - \text{CO} - \text{C}_9\text{H}_{19}$, ethyl nonyl ketone

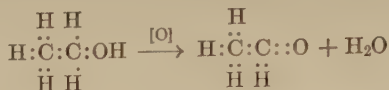
etc.

As with ethers, so with ketones: there are simple and mixed ketones. When $\text{R} = \text{R}'$, we have a simple ketone; when R is different from R' , we have a mixed ketone; so that $\text{C}_2\text{H}_5 \cdot \text{CO} \cdot \text{C}_2\text{H}_5$ is a simple ketone, and $\text{C}_2\text{H}_5 \cdot \text{CO} \cdot \text{C}_4\text{H}_9$ is a mixed ketone.

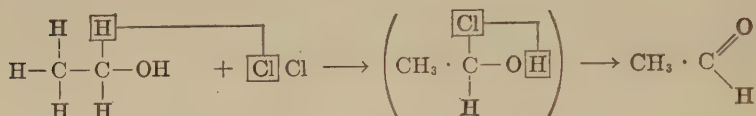
Preparation of Aldehydes and Ketones. 1. The oxidation of a primary alcohol yields an aldehyde; e.g.,



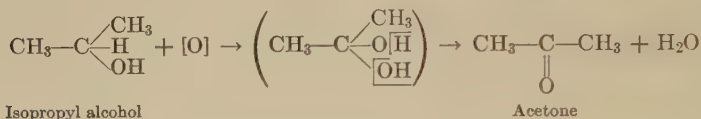
This reaction may be represented as



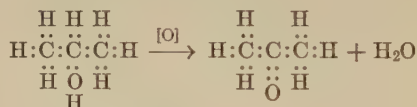
Chlorine acts as an oxidizing agent. For example,



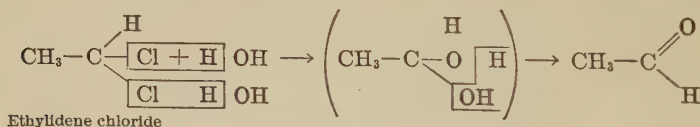
The oxidation of a secondary alcohol yields a ketone; e.g.,



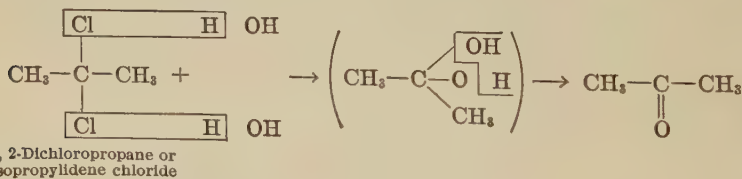
This reaction may be represented as



2. Hydrolysis of dihalogenated hydrocarbons can also be employed to produce carbonyl compounds; e.g.,

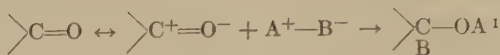


$\text{CH}_2\text{Cl}-\text{CH}_2\text{Cl}$ is ethylene chloride, but $\text{CH}_3 \cdot \text{CHCl}_2$ is ethylidene chloride.

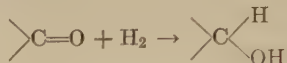


We may note in passing that the hydrolysis of olefin ozonides and the catalytic hydration of acetylenes yield carbonyl compounds.

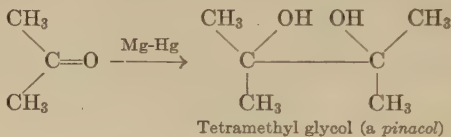
1. The >C=O group acts as an unsaturated group, and its double bond symbolizes certain types of addition. The addition is directed, yielding only one of the two possible products, and may be summarized as follows:



Aldehydes and ketones add hydrogen to form the corresponding primary and secondary alcohols:

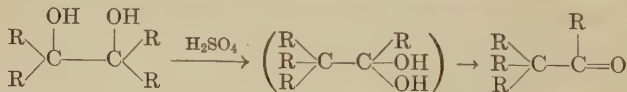


Reducing agents like sodium or magnesium amalgam, or sodium in alcohol or wet ether, produce the same result. Ketones, however, also yield another type of product, particularly when reduced by amalgams or electrolysis:

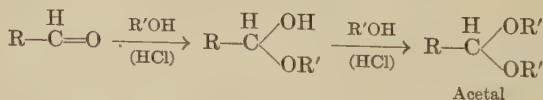


The pinacol from acetone produces on dehydration a diolefin (2,3-dimethylbutadiene) which polymerizes to an elastomer known as "methyl rubber."

Upon heating with sulfuric acid, pinacols produce ketones, known as *pinacolones*, whose formation is the result of a molecular rearrangement:



Alcohols react with aldehydes to give *acetals*, whose formation may be interpreted as the addition of one mole to a carbonyl group followed by reaction with another mole of alcohol:

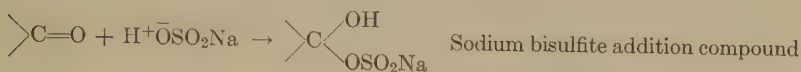


Acetals, although they are written with ether linkages, are hydrolyzed to aldehydes and alcohols by acid. Ketones do not react with alcohols but with thioalcohols (p. 213) to yield similar structures.

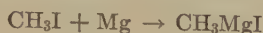
Important addition products are obtained with other substances. Aldehydes and simple ketones, those having a methyl group or at least

¹ Polarity, see p. 13.

a methylene (CH_2) group next to the carbonyl group, yield insoluble compounds with hydrogen cyanide and sodium bisulfite:

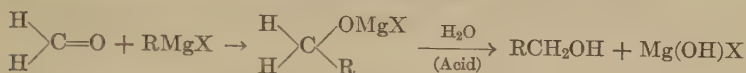


Addition compounds may also be obtained with **Grignard reagents**. A simple example of a *Grignard* reagent is $\text{CH}_3 \cdot \text{Mg} \cdot \text{I}$, methyl magnesium iodide, prepared by the action of magnesium on methyl iodide:

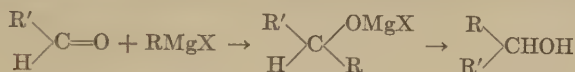


and, in general, the *Grignard* reagent may be written as RMgX .

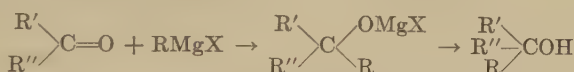
With aldehydes and ketones the *Grignard* reagent first forms addition compounds which may subsequently be converted into various alcohols. With formaldehyde a primary alcohol is ultimately obtained:



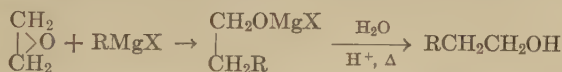
With an aldehyde other than formaldehyde one gets a secondary alcohol:



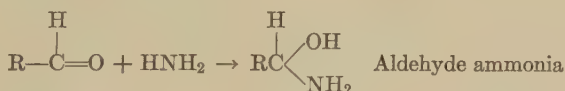
Ketones yield tertiary alcohols:



It may be pointed out at this stage that primary alcohols can also be synthesized from RMgX through addition to ethylene oxide (p. 80), which, incidentally, adds many other carbonyl reagents:

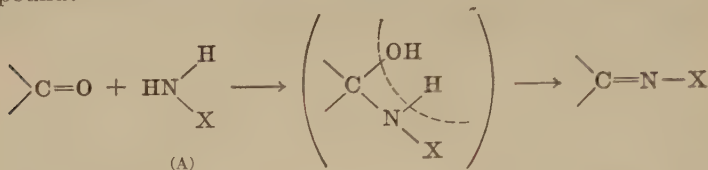


Ammonia forms simple products with aldehydes but complex condensation products with ketones.



On the other hand, several derivatives of ammonia yield insoluble compounds with aldehydes and ketones. These are crystalline and serve to identify the corresponding carbonyl compounds. They may

be assumed to result from the elimination of water from the addition compound:



Where (A) is NH_2OH , hydroxylamine, we get >C=NOH , an oxime (Victor Meyer). Where (A) is $\text{H}_2\text{NNHC}_6\text{H}_5$, phenylhydrazine,¹ we get $\text{>C=NNHC}_6\text{H}_5$, a phenylhydrazone. Where the (A) is $\text{H}_2\text{NNHCONH}_2$, semicarbazide, we get >C=NNHCONH_2 , a semicarbazone.

2. Aldehydes are oxidized readily to carboxylic acids by oxidizing agents. Weak oxidizing agents such as *Tollens'* reagent ($\text{Ag}(\text{NH}_3)_2^+$) and *Fehling's* reagent (Cu^{++} in alkaline solution, p. 196) are specific for the aldehyde function, $\text{—C} \begin{array}{c} \text{H} \\ \text{=O} \end{array}$.

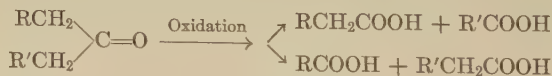


Aldehydes are oxidized and reduced rather readily and can be made to undergo a simultaneous oxidation and reduction:³



This reaction is catalyzed by metallic alkoxides like $\text{Al}(\text{i-C}_3\text{H}_7\text{O})_3$.

Ketones are rather resistant to oxidation. Only strong oxidizing agents such as alkaline KMnO_4 and chromic anhydride (CrO_3) in H_2SO_4 have any effect. If mixed ketones are used, two pairs of carboxylic acids are obtained:



3. The hydrogen atoms on the carbon atom next to the carbonyl group, known as the alpha (α) carbon, show increased reactivity,

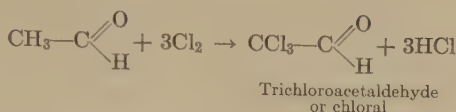
¹ Phenylhydrazine is hydrazine, $\text{H}_2\text{N—NH}_2$, wherein one hydrogen has been replaced by the monovalent C_6H_5 (phenyl) group (p. 241). The phenyl group bears the same relationship to benzene that the methyl group does to methane.

² Some of the oxidizing agents and the changes which they undergo are: $\text{Cr}_2\text{O}_7^{= -} \rightarrow \text{Cr}^{+++}$; $\text{MnO}_4^- \xrightarrow{\text{OH}^-} \text{MnO}_2$; $\text{MnO}_4^- \xrightarrow{\text{H}^+} \text{Mn}^{++}$; $\text{Ag}(\text{NH}_3)_2^+ \rightarrow \text{Ag}^\circ$ (Mirror); $\text{Cu}^{++} \xrightarrow{\text{OH}^-} \text{Cu}_2\text{O}$ (Red precipitate).

³ Recall the inorganic reaction $\text{Na}_2\text{SO}_3 \rightarrow \text{Na}_2\text{S} + \text{Na}_2\text{SO}_4$.

especially in alkaline media. The proximity of the negative $C=O$ group renders the hydrogen more mobile and therefore more easily removable by bases (p. 15).

Halogens replace α -hydrogens readily:



Since chlorine oxidizes ethanol to acetaldehyde, chloral is prepared on a large scale from the alcohol.

A halogen in alkaline solution (hypohalite) not only effects the substitution shown above, but also splits the bond between the α -carbon and the carbonyl carbon.



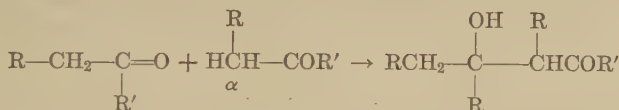
With acetone, for example, the reaction is



This type of reaction is specific for compounds of the structure CH_3COR —acetaldehyde and methyl ketones—and it produces the haloform, CHX_3 , and the salt of an acid, $RCOONa$.

Since hypohalites are good oxidizing agents, ethanol and the alcohols of the type CH_3CHOHR are oxidized to the corresponding carbonyl structures which then give the reaction just described, which is known as the **haloform reaction**.

In dilute alkali, the active hydrogens also add to the oxygen of the carbonyl group of another molecule of aldehyde or ketone to form dimers known as *aldols*.



This *aldol condensation* occurs only if at least one α -hydrogen is present. It yields some useful compounds and serves, among other things, as a working hypothesis to explain the conversion of sugars into fats in the animal body. The same mechanism may also account for the polymerization of aldehydes to resins in alkaline solution, as well as for the formation of some definite polymers of aldehydes and ketones.

For a summary of a number of reactions of aldehydes and ketones, see pp. 92-94.

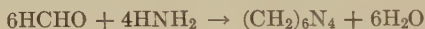
ALDEHYDES

Formaldehyde, $\text{H} \cdot \text{CHO}$ (methanal), is manufactured by passing methanol vapor and air over copper gauze:



The reaction is exothermic, and the copper need not be heated except to start the reaction. Formaldehyde is a gas with an irritating odor, soluble in water. The **formalin** of commerce is a 35–40 per cent aqueous solution of the gas. A small amount of methanol must be present in the formalin to prevent polymerization of the formaldehyde. For disinfecting purposes, specially constructed lamps are used containing methanol, which when burnt (in the presence of copper or platinum) yields formaldehyde. Formaldehyde is used as a food preservative, disinfectant, and germicide, both in the form of gas and in solution. In the manufacture of dyes such as indigo, the hardening of photographic films, the preservation of tissues (hardening the albuminous material), the manufacture of synthetic resins such as Bakelite (see the chapter on phenol, p. 279) and urea-formaldehyde resins, formaldehyde finds uses.¹

Ammonia and formaldehyde combine to form hexamethylene-tetramine:



commonly known also as urotropine, "aminoform," or "methenamine," which finds use as a urinary antiseptic, liberating formaldehyde (in acid fluids only); it is also used in the manufacture of synthetic resins.

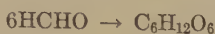
It is believed that, in the formation of sugars from carbon dioxide and moisture (in the plant kingdom), formaldehyde may be an intermediate product. *Emil Fischer* obtained a sugar (acrose) by treating formaldehyde with barium or calcium hydroxide, thereby forming "formose" (a mixture of sugars), and isolating the acrose from the formose.

¹ All plastics are synthetic resins, but the reverse is not necessarily true.

Both Bakelite and synthetic rubber are synthetic resins, but Bakelite alone is a plastic. Plastics can be molded into various shapes under heat and pressure, giving rise to stable forms. On the other hand, rubber, though plastic while being formed, once prepared is still capable of deformation and elastic recovery.

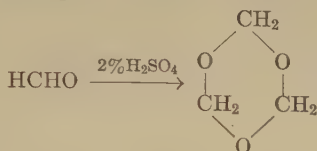
Resins, of which Bakelite is an example, will be referred to again in various parts of the book, but a word or two regarding the general properties of plastics may be added here. Plastics are highly resistant to chemical and atmospheric action. They are light and can be prepared in various colors. Some are transparent, others translucent, and still others opaque. Plastics still cannot compete with metals in such properties as hardness, heat, resistance, and structural strength.

The conversion of formaldehyde into a sugar involves polymerization; it may be represented as



Another polymer of formaldehyde may be obtained by treating the substance with sulfuric acid and evaporating the solution. The paraformaldehyde (also known as "paraform") so obtained is a solid mixture of hydrated formaldehyde linear polymers with the formula $\text{HO}(\text{CH}_2\text{O})_n\text{H}$, where n varies from 10 to 100. The formaldehyde gas may again be obtained by simply heating this polymerized formaldehyde. There are lamps on the market which liberate formaldehyde in this way.

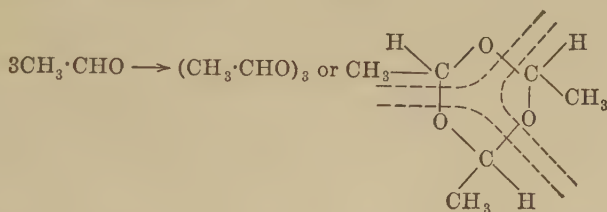
There are other polymers of formaldehyde, linear as well as cyclic. One of the most interesting of the cyclic is trioxane, whose structure is that of a six-membered ring:



It is a stable compound from which anhydrous formaldehyde can be obtained slowly by heating with strong acids.

Acetaldehyde, $\text{CH}_3 \cdot \text{CHO}$ (ethanal), is manufactured by passing acetylene into dilute H_2SO_4 in the presence of mercury salts (p. 41).

Acetaldehyde may be polymerized, just like formaldehyde. If acetaldehyde is treated with sulfuric acid we get *paraldehyde*:



which, since it does not contain the carbonyl ($>\text{CO}$) group, no longer behaves like an aldehyde. If the temperature is lowered, say to 0° , besides getting paraldehyde (a liquid), we get another polymer, metaldehyde (a solid), with the formula $(\text{CH}_3 \cdot \text{CHO})_4$. Paraldehyde when heated with dilute acids is converted back to acetaldehyde. Paraldehyde is used in medicine as a soporific. It is not nearly so volatile and flammable as acetaldehyde, and for this reason acetaldehyde is often transported in the form of paraldehyde and reconverted into acetaldehyde by distillation with dilute acids.

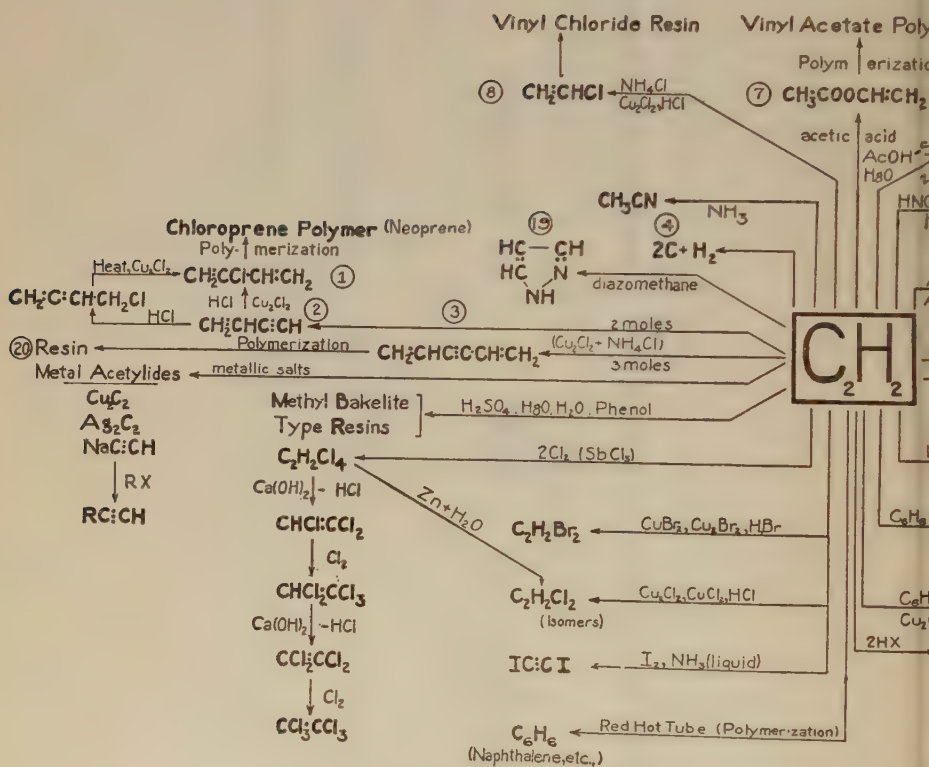
Reagents Used	R·CHO Aldehydes, e.g., CH ₃ ·CHO	R·CO·R Ketones, e.g., CH ₃ ·CO·CH ₃
Oxidation	$\begin{array}{c} \text{H} & \text{O} \\ & \\ \text{H}-\text{C}- & \text{C}-\text{OH} \\ & \\ \text{H} & \end{array}$ <p>Acetic acid</p>	<p>→ Decomposition of molecule producing acids with lower carbon content as H·COOH and CH₃·COOH and CO₂ + H₂O</p>
Reduction	$\begin{array}{c} \text{H} & \text{H} \\ & \\ \text{H}-\text{C}- & \text{C}-\text{OH} \\ & \\ \text{H} & \text{H} \end{array}$ <p>A primary alcohol</p>	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3-\text{C}-\text{OH} \\ \\ \text{H} \end{array} + \begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3-\text{C}-\text{OH} \\ \\ \text{CH}_3 \end{array}$ <p>A secondary alcohol A pinacol (tetramethyl glycol)</p>
$\begin{array}{c} \text{OH} \\ \\ \text{S} \rightarrow \text{O} \\ \\ \text{ONa} \end{array}$ <p>Sodium bisulfite</p>	$\begin{array}{c} \text{OH} \\ \\ \text{CH}_3-\text{C}-\text{CH}_3 \\ \\ \text{OSO}_2\text{Na} \end{array}$ <p>Acetone sodium hydrogen sulfite</p>	<p>→</p>
NH ₃	$\begin{array}{c} \text{H} \\ \\ \text{CH}_3-\text{C}-\text{OH} \\ \\ \text{NH}_2 \end{array}$ <p>Acetaldehyde ammonia</p>	<p>Complex condensation products, in place of an addition compound, are formed</p>

HCN	$\begin{array}{c} \text{H} \\ \\ \rightarrow \text{CH}_3 - \text{C} - \text{OH} \\ \\ \text{CN} \end{array}$ <p>Acetaldehyde hydrogen cyanide or ethylidene cyanohydrin</p>	$\begin{array}{c} \text{OH} \\ \\ \rightarrow \text{CH}_3 - \text{C} - \text{CH}_3 \\ \\ \text{CN} \end{array}$ <p>Acetone hydrogen cyanide</p>
PCl ₅	$\begin{array}{c} \text{H} \\ \\ \rightarrow \text{CH}_3 - \text{C} - \text{Cl} \\ \quad \\ \text{Cl} \quad \text{Cl} \end{array}$ <p>Ethylidene chloride</p>	$\begin{array}{c} \text{Cl} \\ \\ \rightarrow \text{CH}_3 - \text{C} - \text{CH}_3 \\ \quad \\ \text{Cl} \quad \text{Cl} \end{array}$ <p>2,2-Dichloropropane</p>
Halogens	$\begin{array}{c} \text{O} \\ \\ \text{Cl} - \text{C} - \text{Cl} \\ \quad \\ \text{Cl} \quad \text{Cl} \end{array}$ <p>Trichloroacetaldehyde</p> <p>→ substitute in CH₃ group: e.g.,</p>	<p>→ substitute in CH₃ groups: e.g.,</p> <p>CCl₃ · CO · CH₃ Trichloroacetone</p>
H ₂ N · OH Hydroxylamine	$\begin{array}{c} \text{H} \\ \\ \text{CH}_3 \cdot \text{C} = \text{O} + \boxed{\text{H}_2\text{N} \cdot \text{OH}} \end{array}$ <p>Acetaldoxime</p>	$\begin{array}{c} \text{CH}_3 \\ \\ \text{C} = \text{O} + \boxed{\text{H}_2\text{N} \cdot \text{OH}} \rightarrow \text{C} = \text{N} \cdot \text{OH} \\ \quad \\ \text{CH}_3 \quad \text{CH}_3 \end{array}$ <p>Acetoxime</p>
H ₂ N · NH ₂ Hydrazine or aminoamine	$\begin{array}{c} \text{H} \\ \\ \text{CH}_3 \cdot \text{C} = \text{O} + \boxed{\text{H}_2\text{N} \cdot \text{NH}_2} \end{array}$ <p>Acetaldehyde hydrazine</p>	$\begin{array}{c} \text{CH}_3 \\ \\ \text{C} = \text{O} + \boxed{\text{H}_2\text{N} \cdot \text{NH}_2} \rightarrow \text{C} = \text{N} \cdot \text{NH}_2 \\ \quad \\ \text{CH}_3 \quad \text{CH}_3 \end{array}$ <p>Acetone hydrazone</p>

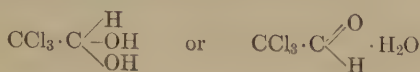
* The =NOH group is known as the "oxime" group.

Reagents Used	Aldehydes, e.g., $\text{CH}_3 \cdot \text{CHO}$	Ketones, e.g., $\text{CH}_3 \cdot \text{CO} \cdot \text{CH}_3$
$\text{H}_2\text{N}-\text{NHC}_6\text{H}_5$ Phenylhydrazine	$\text{CH}_3 \cdot \text{C} \begin{array}{l} \text{H} \\ \diagup \end{array} = \boxed{\text{O} + \text{H}_2\text{N} \cdot \text{NHC}_6\text{H}_5} \rightarrow \text{CH}_3 \cdot \text{C} \begin{array}{l} \text{H} \\ \diagup \end{array} = \text{N} \cdot \text{NHC}_6\text{H}_5$ Acetaldehyde phenylhydrazone	$\text{CH}_3 \cdot \text{C} \begin{array}{l} \text{CH}_3 \\ \diagup \end{array} = \boxed{\text{O} + \text{H}_2\text{N} \cdot \text{NHC}_6\text{H}_5} \rightarrow \text{CH}_3 \cdot \text{C} \begin{array}{l} \text{CH}_3 \\ \diagup \end{array} = \text{N} \cdot \text{NHC}_6\text{H}_5$ Acetone phenylhydrazone
$\text{C}_2\text{H}_5\text{OH}$ (In presence of a dehydrating agent, such as HCl gas)	$\text{CH}_3 \cdot \text{C} \begin{array}{l} \text{H} \\ \diagup \end{array} = \boxed{\text{O} + \text{H} \cdot \text{OC}_2\text{H}_5} \rightarrow \text{CH}_3 \cdot \text{C} \begin{array}{l} \text{H} \\ \diagup \end{array} = \text{C} \begin{array}{l} \text{OC}_2\text{H}_5 \\ \diagup \end{array} \text{OC}_2\text{H}_5$ Acetal or ethylidene diethyl ether	No similar reaction
<i>Tollens'</i>	Aldehydes reduce ammoniacal silver nitrate solution to produce silver mirror	Ketones do not reduce the reagent

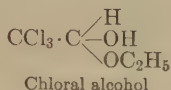
Chart of Products



Chloral (p. 89) is an oily liquid with a penetrating smell. It reacts with water, forming **chloral hydrate**,

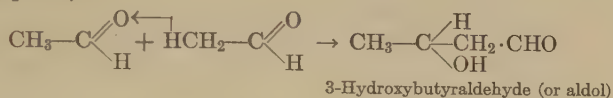


which is used as a soporific. In large doses, it acts as an anesthetic. Chloral also combines with alcohol to form a crystalline substance



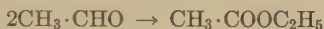
Bromal, $\text{CBr}_3 \cdot \text{CHO}$, and iodal, $\text{CI}_3 \cdot \text{CHO}$, are also known.

By means of dilute alkali or of zinc chloride solution, two molecules of acetaldehyde condense to aldol, a derivative of butyraldehyde (see chart facing p. 94).



Hydrogenation of aldol yields 1,3-butyleneglycol which can be dehydrated to butadiene, one of the starting points for the manufacture of synthetic rubber. This gives us a means of manufacturing rubber from ethyl alcohol.

Two molecules of acetaldehyde can be catalytically condensed into ethyl acetate (see chart facing p. 94).



Butyraldehyde, butanal, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CHO}$, is the most important of the higher aldehydes used in the preparation of rubber accelerators and synthetic resins.

Higher aldehydes up to C_{22} are used in the preparation of synthetic perfumes and artificial fruit flavors.

Aldehydes are detected (a) by reduction of an ammoniacal silver nitrate solution to silver (silver mirror) (*Tollens' test*); (b) by the reduction of alkaline copper sulfate solution (*Fehling's test*), giving red cuprous oxide; (c) by the formation of a reddish violet color with magenta solution which has been decolorized by SO_2 (*Schiff's test*).

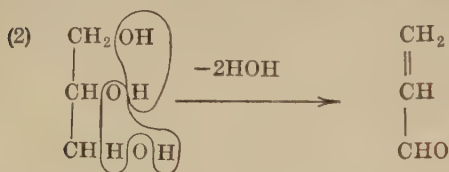
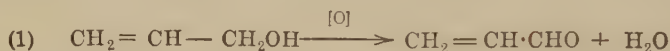
Glyoxal, $\begin{array}{c} \text{CHO} \\ | \\ \text{CHO} \end{array}$, is a dialdehyde. Its dimethyl derivative is dimethyl glyoxal, $\begin{array}{c} \text{CH}_3 \cdot \text{C}=\text{O} \\ | \\ \text{CH}_3 \cdot \text{C}=\text{O} \end{array}$, the dioxime of which is dimethyl glyoxime,

$\begin{array}{c} \text{CH}_3-\text{C}=\text{NOH} \\ | \\ \text{CH}_3-\text{C}=\text{NOH} \end{array}$, a substance used in the gravimetric determination of nickel.

Unsaturated Aldehydes. Acrylaldehyde or propenal,

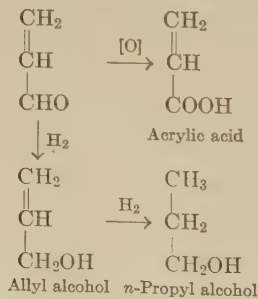


commonly called **acrolein**, is prepared either (1) by the oxidation of allyl alcohol, or (2) by the dehydration of glycerol with KHSO_4 or anhydrous MgSO_4 , or (3) by heating fats and oils to a somewhat high temperature.



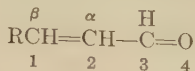
The odor of burning fat is mainly due to acrolein. On account of its lachrymatory property it is used as a warning agent in toxic gases.

The properties of acrolein are those of an unsaturated compound and of an aldehyde; and so we get reactions such as these:



Crotonaldehyde, $\text{CH}_3\cdot\text{CH}=\text{CH}\cdot\text{CHO}$, prepared by the dehydration of aldol, is used in the manufacture of rubber accelerators; as an insecticide; for the detection of leaks in gas supplies; and as a constituent of tear-gas shells and bombs.

Acrolein and crotonaldehyde are α,β -unsaturated aldehydes in which there is a conjugated double bond structure (p. 43):



Many of their reactions can be readily explained on that basis. Such conjugation also accounts for the stability of many α,β -unsaturated compounds.

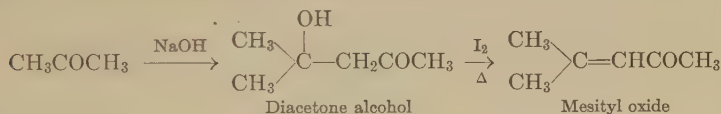
KETONES

Acetone, CH_3COCH_3 (propanone, dimethyl ketone), is prepared commercially by the catalytic dehydrogenation of isopropyl alcohol from the products obtained in the cracking process and in the fermentation of corn (*Weizmann* process), and by heating (pyrolysis) calcium acetate. This liquid has a characteristic odor, a peppermint-like taste, and is miscible with water (b.p. 56.1°). It is flammable.

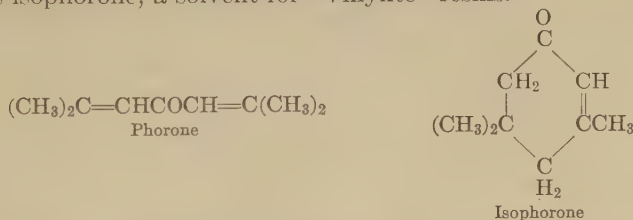
Acetone finds its greatest use as a solvent: in acetylene cylinders (as a solvent for the gas), in the production of acetate rayon, artificial leather, photographic films, pyroxylin plastics, smokeless powder, airplane and leather "dopes," lacquers, paint and varnish removers, dry-cleaning, etc.

As a raw material, acetone is used in the manufacture of chloroform, iodoform, sulfonal (p. 215), indigo (p. 335), and various resins and plastics.

By an aldol condensation, acetone yields diacetone alcohol, a useful solvent. Dehydration of this compound yields mesityl oxide:



A similar condensation of acetone in the presence of HCl yields mesityl oxide and, by further condensation, phorone. Still another condensation produces isophorone, a solvent for "Vinylite" resins.

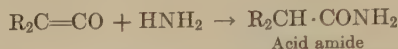
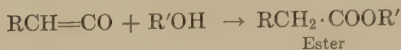
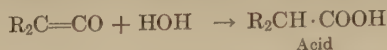


Acetone is present in the urine and in the breath of persons suffering from severe diabetes.

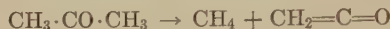
Higher ketones up to C_{22} are used in the preparation of synthetic perfumes and artificial fruit flavors. Many find use as solvents in lacquers, synthetic resin finishes, etc.

Ketene is $\text{CH}_2=\text{C}=\text{O}$. Aldoketenes have the formula $\text{RCH}=\text{C}=\text{O}$, and ketoketenes $\text{R}_2\text{C}=\text{C}=\text{O}$. They are very unstable and reactive

substances. They readily add water, alcohols, amines, ammonia, acids, etc.



When acetone vapor is passed over clay chips heated to 700° , or over a glowing platinum wire, ketene is formed:



QUESTIONS

- What characteristic reactions serve to differentiate the aldehydes from the ketones?
- Write structural formulas for (a) propanal; (b) acetaldoxime; (c) glyoxal; (d) aldol; (e) acrolein; (f) ketene; (g) chloral; (h) 2-hexanone; (i) pinacol; (j) isobutyraldehyde; (k) isopropyl isobutyl ketone.
- Show, by means of equations, how ethanal can be converted into (1) CH_3CHCl_2 ; (2) $\text{CH}_3\cdot\text{CHOH}\cdot\text{CH}_3$; (3) $\text{CH}_3\cdot\text{CHOH}\cdot\text{CN}$; (4) $\text{CH}_3\cdot\text{CHOH}\cdot\text{CH}_2\cdot\text{CHO}$.
- Show, by means of equations, how acetone can be converted to (1) $\text{CH}_3\cdot\text{CHOH}\cdot\text{CH}_3$; (2) $(\text{CH}_3)_3\text{C}\cdot\text{OH}$; (3) $\text{CH}_3\cdot\text{CCl}_2\cdot\text{CH}_3$; (4) $(\text{CH}_3)_2=\text{COH}\cdot\text{COH}=(\text{CH}_3)_2$; (5) $\text{CH}_2=\text{CO}$.
- Show, by means of equations, how you could readily differentiate between (1) $\text{CH}_3\cdot\text{CH}_2\cdot\text{CHO}$ and $\text{CH}_2=\text{CH}\cdot\text{CHO}$; (2) $\text{CH}_3\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CHO}$ and $\text{CH}_3\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CH}_3$; (3) $(\text{C}_2\text{H}_5)_2=\text{CHOH}$ and $(\text{C}_2\text{H}_5)_2=\text{CO}$.
- Write complete equations (when possible), and name the products formed, when acetaldehyde and acetone are treated with the following reagents: (a) HCN ; (b) NH_3 ; (c) sodium bisulfite; (d) hydroxylamine; (e) hydrazine; (f) methyl magnesium bromide; (g) chlorine; (h) phenylhydrazine; (i) ethanol in the presence of HCl ; (j) PCl_5 ; (k) oxidizing agent; (l) reducing agent.
- Outline the different modes of behavior of an unsaturated aldehyde toward the following reagents: H_2 , Cl_2 , HBr , O_2 .
- Write equations for the preparation of the following compounds:

(a) propionaldehyde	from 1,1-dichloropropane
(b) trichloroacetaldehyde	" acetaldehyde
(c) ethylidene chloride	" acetaldehyde
(d) ethyl methyl carbinol	" ethanol
(e) ethanol	" acetaldehyde
(f) acetone	" methylacetylene
(g) triethyl carbinol	" 3-pentanone and ethanol
(h) acetaldehyde cyanohydrin	" acetylene
(i) acetone	" acetic acid
(j) chloroform	" acetone
(k) ketene	" acetone
(l) acetone	" isopropanol
(m) propionaldehyde	" calcium propionate
(n) <i>n</i> -amyl alcohol	" <i>n</i> -propyl alcohol and C_2H_4

CHAPTER VIII

CARBOXYLIC ACIDS

An organic acid of this class contains the "carboxyl" group,¹



and may be regarded as a hydrocarbon in which one or more of the hydrogens is replaced by COOH groups; e.g., $\text{CH}_3\text{H}-\text{CH}_3\cdot\text{COOH}$. If the compound contains one COOH group, it is known as a monobasic acid; if two such groups, dibasic; if three, tribasic; etc. We have analogous types in inorganic chemistry; e.g., HCl , H_2SO_4 , H_3PO_4 , etc.

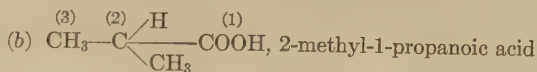
Nomenclature. Several acids have names that suggest their origin (formic from "formica," butyric from butter, valeric from "valeriana," palmitic from palm oil, etc.). The acids may also be named in the Geneva system by changing the ending *-e* of the hydrocarbons containing the same number of carbon atoms to *-oic*, so that

CH_4 , methane, becomes $\text{H}\cdot\text{COOH}$, methanoic acid

C_2H_6 , ethane, becomes $\text{CH}_3\cdot\text{COOH}$, ethanoic acid

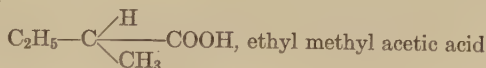
C_3H_8 , propane, becomes $\text{CH}_3\cdot\text{CH}_2\cdot\text{COOH}$, propanoic acid

C_4H_{10} , butane, becomes (a) $\text{CH}_3-\text{CH}_2-\text{CH}_2-\text{COOH}$, butanoic acid

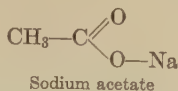
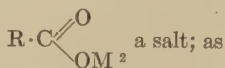


The acids may be named as derivatives of acetic acid, $\text{CH}_3\cdot\text{C}\begin{array}{l} \text{O} \\ \parallel \\ \backslash \\ \text{OH} \end{array}$;

e.g.,

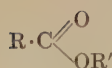


Types of Acid Derivatives. Acids in which some element or group has been substituted in the OH of the COOH group are called "acid derivatives" (they will be taken up later):

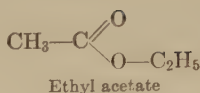


¹ Other groups, like SO_3H , etc., are also acid groups.

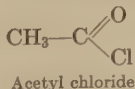
² M = metal.



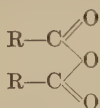
an ester; as



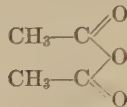
an acyl halide; as



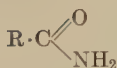
The $\text{R} \cdot \text{C} \begin{array}{l} \text{O} \\ // \\ \text{O} \end{array}$ group is known as an "acyl" group; $\text{CH}_3 \cdot \text{C} \begin{array}{l} \text{O} \\ // \\ \text{O} \end{array}$ is the acetyl group.



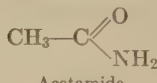
an acid anhydride; as



Acetic anhydride



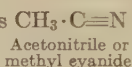
an acid amide; as



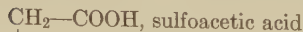
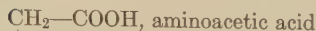
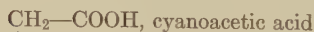
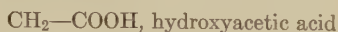
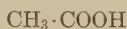
Acetamide



an acid nitrile or alkyl cyanide; as



Types of Substituted Acids. Acids in which the COOH groups remain unchanged but in which substitution has taken place in the residual groups, R , are known as substituted acids.

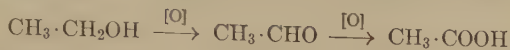


The SO_3H group is known as the sulfonic acid group or sulfo group.

The student should at this point thoroughly familiarize himself with these type compounds, as frequent allusion will be made to them.

MONOBASIC ACIDS (FATTY ACID SERIES¹), R—COOH

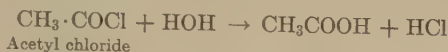
General Methods of Preparation. 1. Oxidation of a primary alcohol, or of an aldehyde; e.g.,



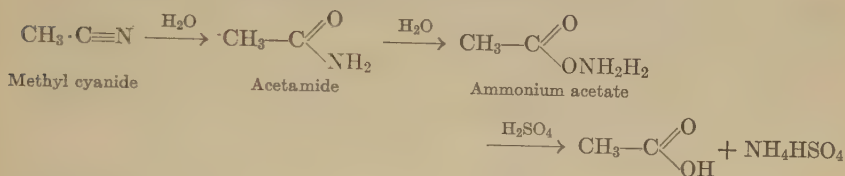
2. Hydrolysis of esters (in presence of acids or alkalies); e.g.,



3. Hydrolysis of acyl halides; e.g.,



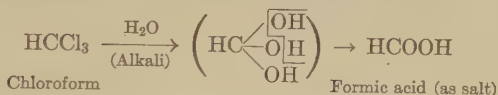
4. Hydrolysis of alkyl cyanides or of acid amides; e.g.,



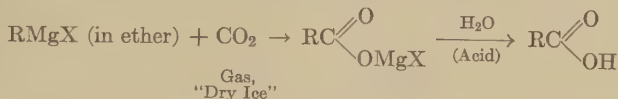
The CN group hydrolyzes to a COOH group.

Throughout the book, statements will be seen to the effect that the CN group is hydrolyzed to the COOH group by the use of H₂O. They should be taken as meaning that either acid or alkali is usually present. This is true of most hydrolytic reactions.

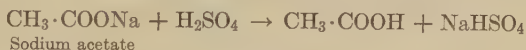
5. Hydrolysis of alkyl 1,1,1-trihalides; for example,



6. Addition of *Grignard* reagents to carbon dioxide and hydrolysis of the resulting complex; for example,



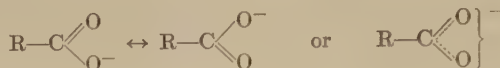
7. Decomposition of salts of organic acids with mineral acids; e.g.,



¹ Named *fatty acids* because many of them are contained in fats or are formed from fats on hydrolysis.

General Properties. The lower members up to $C_9H_{19}\cdot COOH$ are liquids with strong odors, and the higher ones, waxy solids. They are stable substances and difficult to oxidize or reduce. They ionize to a slight extent (e.g., $CH_3COO^-H^+$), but their salts ionize quite considerably.

The stability of these anions is readily explained in terms of resonance (p. 56).

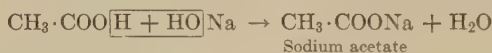


It is interesting to note too that, whereas the acids are quite resistant to reduction, derivatives such as the esters, amides, etc., of the type

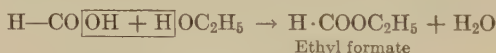
$R-\overset{\overset{O}{\parallel}}{\underset{\underset{X}{\parallel}}{C}}$, in which no resonance is possible, yield the corresponding primary alcohols readily.

The monocarboxylic acids form:

(a) Salts with bases; e.g.,



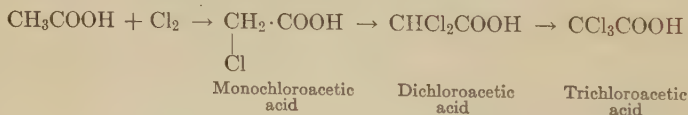
(b) Esters with alcohols; e.g.,



(c) Acyl chlorides with PCl_5 or $SOCl_2$; e.g.,

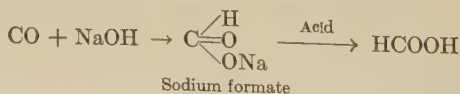


(d) Halogen substitution products (where halogen substitutes in the alkyl group); e.g.,



Formic acid, $HCOOH$ (methanoic acid), is a colorless liquid with an odor resembling that of sulfur dioxide. It is the strongest acid of this series. It occurs in bees, ants, nettles, and pine needles. The "stinging" by bees is due to penetration of formic acid under the skin.

Formic acid is manufactured by heating sodium hydroxide to 150° - 170° with carbon monoxide under 6-7 atmospheres:

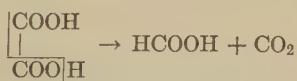


NORMAL FATTY ACIDS *

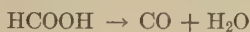
Name	Formula
Formic acid	H·COOH
Acetic acid	CH ₃ ·COOH
Propionic acid	C ₂ H ₅ ·COOH
Butyric acid	C ₃ H ₇ ·COOH
Valeric acid	C ₄ H ₉ ·COOH
Caproic acid	C ₅ H ₁₁ ·COOH
Heptoic (oenanthic) acid	C ₆ H ₁₃ ·COOH
Caprylic acid	C ₇ H ₁₅ ·COOH
Nonylic (pelargonic) acid	C ₈ H ₁₇ ·COOH
Capric acid	C ₉ H ₁₉ ·COOH
Undecylic acid	C ₁₀ H ₂₁ ·COOH
Lauric acid	C ₁₁ H ₂₃ ·COOH
.	.
.	.
.	.
Myristic acid	C ₁₃ H ₂₇ ·COOH
.	.
.	.
.	.
Palmitic acid	C ₁₅ H ₃₁ ·COOH
Margaric acid	C ₁₆ H ₃₃ ·COOH
Stearic acid	C ₁₇ H ₃₅ ·COOH
.	.
.	.
.	.
Arachidic acid	C ₁₉ H ₃₉ ·COOH
.	.
.	.
.	.
Melissic acid	C ₂₉ H ₅₉ ·COOH

* For sources of these acids, see chapter on fats (p. 122).

In the laboratory, it is prepared by heating oxalic acid with glycerol. The reactions involved are somewhat complex, but they may be summarized thus:

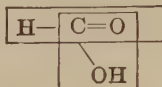


When formic acid is heated with sulfuric acid, carbon monoxide and water are formed:



CO cannot be regarded as the anhydride of HCOOH since CO mixed with water does not give formic acid.

Formic acid is a reducing agent. This may be explained on the theory that it contains an aldehyde (CHO) as well as an acid (COOH) group:



Formic acid is used in the manufacture of dyestuffs, in dyeing and finishing of textiles, in tanning, etc.

Acetic acid, $\text{CH}_3\cdot\text{COOH}$ (ethanoic acid), occurs in fruits and oils in the form of esters. The common dilute form, known as **vinegar**, is produced by the fermentation of fruit juices (such as apple), which contain sugar. The sugar is first converted to alcohol (owing to the presence of the enzyme zymase), giving cider, which is oxidized to acetic acid by oxidizing bacteria present in the juice. For large-scale production, dilute (6–9 per cent) alcoholic liquor (product of fermentation) is allowed to trickle over beechwood shavings, which are impregnated with *Bacterium aceti*, or with mother of vinegar. Air is admitted on the side of the vats to oxidize the $\text{C}_2\text{H}_5\text{OH}$ to $\text{CH}_3\cdot\text{COOH}$. The temperature is kept at about 35° . After the conversion of the alcohol to acetic acid, the product is sold as vinegar.

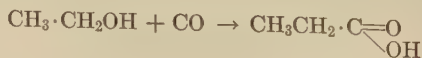
Vinegar contains about 3–6 per cent of acetic acid; it also contains other acids (derived from fruit), esters, albuminous matter, etc. A higher concentration of acid is obtained from “pyroligneous acid,” which contains acetic acid (4–10 per cent), this being separated from the other constituents of pyroligneous acid by conversion into calcium acetate $(\text{CH}_3\text{COO})_2\text{Ca}$ and subsequent liberation of the acid by the addition of sulfuric acid.

Synthetic acetic acid for industrial purposes is now made mainly by the catalytic oxidation of acetaldehyde (using manganese acetate as the catalyst), which, in turn, is made from acetylene.

Glacial acetic acid is anhydrous acetic acid; as its name implies, it resembles ice when frozen ($+16^\circ\text{C}$).

Acetic acid is used as a solvent and to prepare acetates. It is also employed in the manufacture of dyes, drugs (like acetanilide), and white lead.

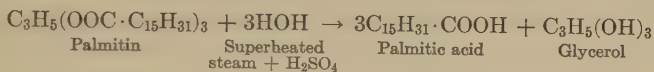
Propionic acid, $\text{C}_2\text{H}_5\cdot\text{COOH}$, is present in small amounts in pyroligneous acid. It may be prepared by the following reaction employing a catalyst:



Butyric acid, $\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{COOH}$, occurs in two forms: as the normal and the iso, $\begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} \rangle \text{CH} \cdot \text{COOH}$. The normal variety is present in rancid butter, muscle, sweat, cheese, feces, etc. It has a disagreeable odor. (Calcium *n*-butyrate is one of the few substances more soluble in cold than in hot water.)

Isovaleric acid, $\begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} \rangle \text{CH} \cdot \text{CH}_2 \cdot \text{COOH}$, occurs in angelica and valerian roots.

Palmitic acid, $\text{C}_{15}\text{H}_{31} \cdot \text{COOH}$, and **stearic acid**, $\text{C}_{17}\text{H}_{35} \cdot \text{COOH}$, are widely distributed, accompanied by oleic acid, $\text{C}_{17}\text{H}_{33} \cdot \text{COOH}$, in most animal and vegetable oils and fats, as the glyceryl esters. (See Chapter X.) From these esters the acids are obtained by hydrolysis; e.g.,



The stearin candles of commerce consist of a mixture of palmitic with excess of stearic acid; some paraffin is added to prevent crystallization and brittleness.

UNSATURATED MONOCARBOXYLIC ACIDS

Acrylic acid, $\text{CH}_2=\text{CH} \cdot \text{COOH}$ (propenoic acid), shows characteristic properties due to its double bond and to its carboxyl group.

Crotonic acid, $\text{CH}_3-\text{CH}=\text{CH} \cdot \text{COOH}$, derives its name from croton oil. Both of these acids are α,β -unsaturated acids of conjugated double-bond structure.

Oleic acid, $\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$ ($\text{C}_{17}\text{H}_{33} \cdot \text{COOH}$), present as the glyceryl ester in fats and oils (p. 122), is usually found associated with palmitic and stearic acids. Oleic acid is a liquid; on a large scale it is separated from the solid palmitic and stearic acids by squeezing it out under hydraulic pressure. Commercial oleic acid, known as "red oil," is used for the manufacture of soap, greases, in the dry-cleaning industry, etc. It is an unsaturated acid. With hydrogen, it is converted into the saturated stearic acid.

Ricinoleic acid, $\text{CH}_3(\text{CH}_2)_5\text{CHOHCH}_2\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$, as a glyceryl ester, is the principal component of castor oil.

Linoleic acid, $\text{C}_{17}\text{H}_{31}\text{COOH}$, contains two double bonds. It is present in the form of a glyceryl ester in linseed oil and other drying oils.

Linolenic acid, $\text{C}_{17}\text{H}_{29}\text{COOH}$, contains three double bonds. It is present in the form of a glyceryl ester in linseed, tung, and other drying oils.

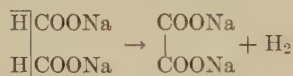
Both linoleic and linolenic acids have been shown to be essential food constituents (in the diet of rats, at least).

DICARBOXYLIC ACIDS, $C_nH_{2n}(COOH)_2$

These compounds are dibasic. They are analogous to H_2SO_4 , which contains two replaceable hydrogens. They are capable of forming two series of salts, viz., acid and normal, and likewise two series of amides, esters, chlorides, etc., as well as mixed derivatives. The general type reactions are analogous to those given for monobasic acids.

Oxalic acid, $\begin{array}{c} COOH \\ | \\ H \\ | \\ COOH \end{array}$, is present, in the form of acid salts (potassium, calcium, etc.) in some plants (*Oxalis* variety). Rhubarb is rich in it. The urine often contains small quantities of calcium oxalate.

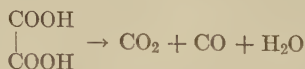
Preparation. Sugars, cellulose, and starch, when oxidized with nitric acid, yield oxalic acid. The commercial method is to heat sawdust with NaOH at 240° , which yields sodium oxalate. Another method is to heat sodium formate (obtained from carbon monoxide and sodium hydroxide) to 400° :



A third method of preparation will be referred to because it is based on a reaction already discussed. When cyanogen is hydrolyzed, oxalic acid is produced:



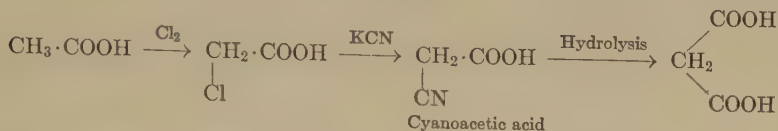
Oxalic acid heated with sulfuric acid yields carbon monoxide, carbon dioxide, and H_2O :



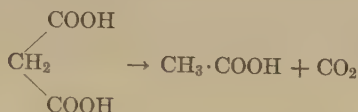
The student will remember the reaction as a laboratory method for the preparation of CO. The CO_2 is removed by passing the mixture of gases through alkali.

Oxalic acid is a strong organic acid. It is used in analytical chemistry as a reducing agent ($C_2O_4^{2-} \rightarrow 2CO_2$). It is also employed in the manufacture of dyes, metal polishes, in bleaching and tanning, etc. It is highly poisonous.

Malonic acid, methanedicarboxylic or 1,3-propanedioic acid, $\begin{array}{c} \text{COOH} \\ | \\ \text{CH}_2 \\ | \\ \text{COOH} \end{array}$, was first obtained by oxidizing malic acid (the acid present in apples). Its synthesis is accomplished as follows:

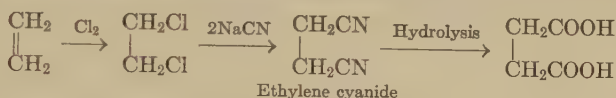


When heated, malonic acid is converted into acetic acid by the loss of CO_2 ,



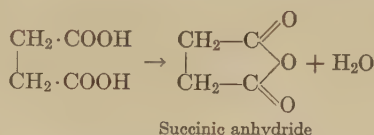
and this proves malonic acid to be a dicarboxylic acid derivative of methane.

Succinic acid, 1,2-ethanedicarboxylic acid, $\begin{array}{c} \text{CH}_2 \cdot \text{COOH} \\ | \\ \text{CH}_2 \cdot \text{COOH} \end{array}$, occurs in amber, in fossil wood, and in the urine of animals. It is produced in processes involving fermentation and may be obtained by distilling amber. Its synthesis may be accomplished thus:

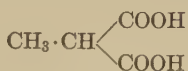


It is made by the hydrogenation of maleic acid (p. 108).

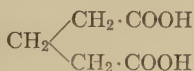
When the acid is heated, it loses a molecule of water and is converted to its anhydride:



Other examples of dibasic acids are methyl malonic acid (isosuccinic acid),

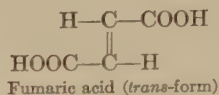
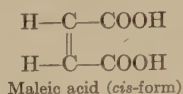


and glutaric acid,

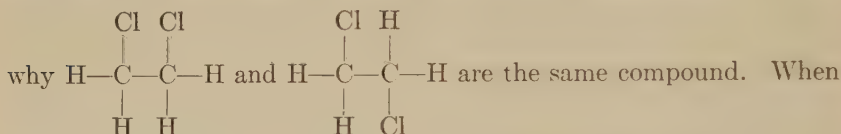


UNSATURATED DICARBOXYLIC ACIDS

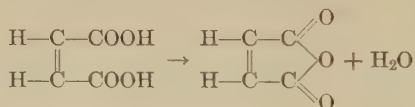
Two compounds with the formula $C_2H_2(COOH)_2$ are known, one being **maleic acid** and the other **fumaric acid**. The formulas ascribed to the two isomers are:



This type of isomerism, known as the "ethylene" or "geometrical" type,¹ is easily understood in terms of the tetrahedral carbon atom. When two tetrahedra are attached by one corner of each they can both spin about an axis passing through this point of attachment. This is



the tetrahedra are attached at two points, however, such spin, or internal rotation, is impossible, and in fumaric acid the two carboxyl groups are permanently on opposite sides of the $C=C$ plane. When maleic acid is heated it produces an anhydride.



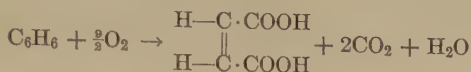
Fumaric acid does not yield an anhydride, which suggests that a compound represented by two COOH groups in juxtaposition has the maleic acid formula. On prolonged heating, however, fumaric acid is converted into maleic acid and anhydride.

The system of nomenclature adopted to distinguish between the two isomers is to term the compound with similar groups on the same side as the *cis* form, and the compound with similar groups on opposite sides on the molecule as the *trans* form.

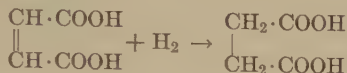
As we can see, any compound of structure $\text{CXY}=\text{CXY}$ (X may be H) can exist in geometrically isomeric forms; this includes olefins like 2-butene, 2- and 3-pentenes, and other 1,2-disubstituted ethylenes, as well as double-bond compounds of every type: for example, crotonic acid and oleic acid. In general, the *trans* forms are more stable than the *cis*.

¹ It is suggested that the instructor show this type of isomerism with atomic models.

Maleic acid is prepared on a commercial scale by the catalytic (V_2O_5) oxidation of benzene vapor by air:



Fumaric acid occurs in various fungi, Iceland moss, etc., and is made by a fermentation process. Maleic acid, on the other hand, is not a natural product, and it is poisonous. Both fumaric and maleic acids on reduction yield succinic acid:



Removal of the double bond removes the possibility of geometrical isomerism.

QUESTIONS

- Show, by means of equations, how isobutyric acid may be prepared from (1) isobutyl alcohol; (2) isopropyl alcohol; (3) *n*-propyl alcohol; (4) isobutyl acetate.
- Write structural formulas for (a) propionic acid; (b) isobutyric acid; (c) acrylic acid; (d) oleic acid; (e) oxalic acid; (f) malonic acid; (g) succinic acid; (h) isosuccinic acid; (i) cyanogen; (j) dimethylacetic acid; (k) maleic acid; (l) fumaric acid; (m) stearic acid.
- Write complete equations (where possible) to represent the reactions which occur when a saturated acid (e.g., acetic acid) and an unsaturated acid (e.g., acrylic acid) are treated with the following: (a) NaOH; (b) C_2H_5OH (HCl gas); (c) I_2 ; (d) HBr; (e) PCl_3 ; (f) NH_3 .
- Name the following: (a) $CH_3 \cdot CH_2 \cdot CHBr \cdot COOH$; (b) $(CH_3)_2CH \cdot COOH$; (c) $CH_2=CH \cdot CH_2 \cdot COOH$.
- Write equations for the preparation of the following compounds:

(a) formic acid	from carbon monoxide
(b) acetic acid	" acetylene
(c) acetic acid	" malonic acid
(d) acetic acid	" methyl iodide (two methods)
(e) acetic acid	" methane
(f) malonic acid	" acetic acid
(g) oxalic acid	" cyanogen
(h) succinic acid	" ethylene
(i) propionic acid	" acrolein
(j) succinic acid	" maleic acid
(k) butyric acid	" <i>n</i> -butyl alcohol
- Show how the structure of acetic acid may be established from its syntheses and from its reactions.

CHAPTER IX

SALTS AND ESTERS OF INORGANIC AND ORGANIC ACIDS

SALTS

Salts of organic acids are important for a number of reasons. In the first place, they are used in the preparation of various organic compounds (see below); then again a number of them are the source of certain elements which the body needs; and finally a group of them belongs to the substances which go under the common name of "soap."

In inorganic chemistry, a salt may be looked upon as an acid in which the acid hydrogen is replaced by a metal; e.g.,

HCl	NaCl	H ₂ SO ₄	NaHSO ₄	Na ₂ SO ₄
Acid	Salt	Acid	Acid salt	Neutral salt

In a similar way, when the acid hydrogen of an organic acid is replaced by a metal, we get a salt:

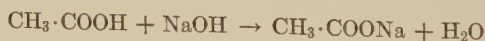
R·COOH	R·COOM ¹
Acid	Salt

For example: CH₃COONa (sodium acetate), (H·COO)₂Cu (copper formate), and C₁₇H₃₃·COONa (sodium oleate).

The naming of these salts is analogous to the naming of inorganic salts:

H ₂ SO ₄	→ Na ₂ SO ₄ ,	sodium sulfate
CH ₃ COOH	→ CH ₃ ·COOK,	potassium acetate
COOH	→ COONa	sodium oxalate
COOH	→ COONa	
CH ₂ ·COOH	→ CH ₂ COO	Cd, cadmium succinate
CH ₂ ·COOH	→ CH ₂ COO	

General Methods of Preparation. Salts are formed by: 1. The action of an acid on a base; e.g.,

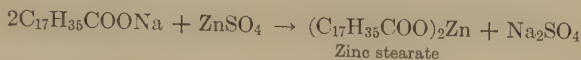


2. The action of an acid on an oxide or a carbonate; e.g.,

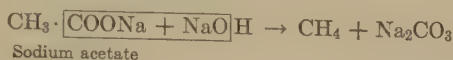


¹ M = metal.

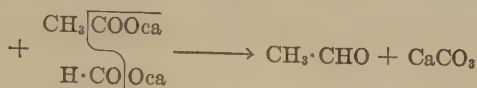
3. The reaction between a water-soluble salt and a salt of a heavy metal; e.g.,



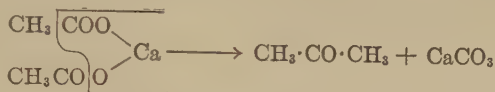
General Properties. These salts are usually crystalline substances and often contain water of hydration. Sodium acetate when heated with soda lime yields methane; e.g.,



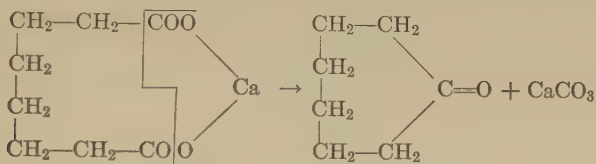
Calcium salts yield aldehydes on pyrolysis with calcium formate:



and ketones on being heated alone:

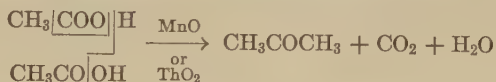


In the case of dicarboxylic acids with six or more carbons, pyrolysis of Ca(Ba, Th) salts yields cyclic ketones:

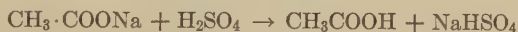


Some of the largest ring structures known have been made by this method.

A similar reaction is the catalytic high-temperature decarboxylation and dehydration of monocarboxylic acids to ketones:

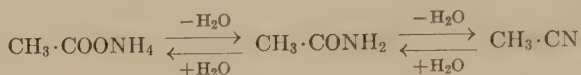


The free acid may be liberated from its salts by the addition of a stronger acid; e.g.,

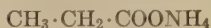
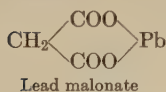
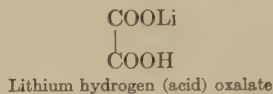
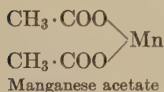
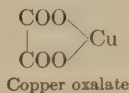


The ammonium salts, when heated with a dehydrating agent, are first converted to the acid amides and then to the cyanides (the reverse

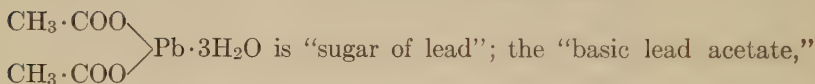
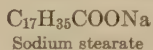
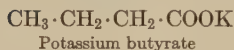
process of converting a cyanide into the acid being one of hydrolysis);
e.g.,



Very many salts are known. Only a few examples will be given:

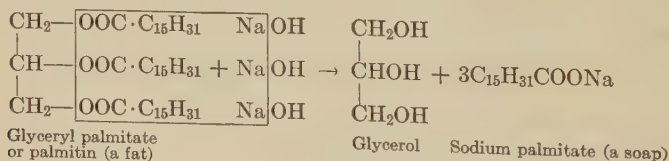


Ammonium propionate

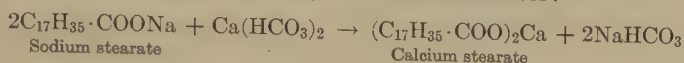


used to purify sugar and many biological substances, is $\text{Pb} \begin{array}{l} \text{OH} \\ \text{OOC} \cdot \text{CH}_3 \end{array}$
"verdigris," or "green pigment," is a combination of copper hydroxide and copper acetate, $\text{Cu}(\text{OH})_2 \cdot (\text{CH}_3\text{COO})_2\text{Cu}$; "Paris green," the insecticide, is a combination of copper arsenite and copper acetate, $(\text{CH}_3\text{COO})_2\text{Cu} \cdot \text{Cu}_3\text{As}_2\text{O}_6$; iron, aluminum, and chromium acetates are used as mordants in dyeing and calico printing.

Soaps. The sodium or potassium salts of some of the higher acids (obtained from fats and vegetable oils), such as palmitic, $\text{C}_{15}\text{H}_{31} \cdot \text{COOH}$, stearic, $\text{C}_{17}\text{H}_{35}\text{COOH}$, and oleic, $\text{C}_{17}\text{H}_{33}\text{COOH}$, are known as **soaps**. Without going into the details of manufacture of these soaps, it may be pointed out that the principle involved is the conversion of the fat or oil, etc., into soap and glycerol by boiling with alkali, and the separation of the soap from the glycerol by a process known as "salting out." This means that salt (NaCl) is added to the mixture, whereupon the soap comes to the surface and is then ladled off. The reaction may be represented thus:



The solid soaps are sodium salts; the soft soaps are mainly potassium salts. Soaps added to "hard" water (containing calcium or magnesium salts in solution) have their sodium replaced by either calcium or magnesium, thereby forming soaps insoluble in water:



This explains the “curds” formed when soap is used in hard water.

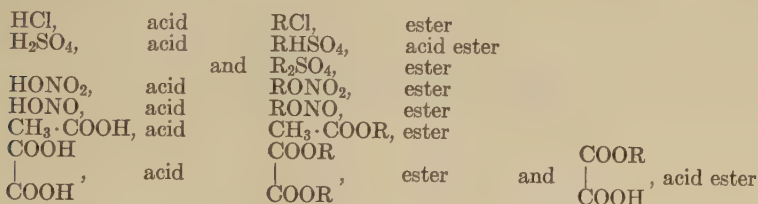
"Lead plaster" is a lead soap made from lead oxide or lead acetate which has been boiled with fat and water. Lead, manganese, or cobalt soaps are used in paints as "driers" to hasten the process of drying. Calcium soaps are used in lubricating greases. Zinc stearate finds extensive use in toilet powders. The "medicated" soaps contain one or more of such substances as phenol (carbolic acid), resorcinol, cresols, salicylic acid, and sulfur. Perfume and coloring materials are often added to soaps.

New types of detergents have been developed in which fatty acids and esters are reduced to the corresponding alcohols. These are converted to the sulfuric acid esters of the alcohols and then to their corresponding sodium salts which are water soluble. Examples of these products are "Dreft," "Gardinol," "Drene," and "Aerosols." The great advantage of these detergents is that, whereas the usual calcium and magnesium soaps are water insoluble, these calcium and magnesium compounds are water soluble. Thus washing in hard or salt water, or in acid or alkaline solution, involves no difficulty because no precipitation takes place. These "sulfate detergents" are effective "wetting agents"; that is, they increase the penetrating power of liquids.

The cleansing action of soaps depends mainly upon the power to emulsify oils and fats, which are then washed away in the form of small globules. As a matter of fact, soap finds extensive use as an emulsifying agent in the manufacture of textiles and of synthetic rubber.

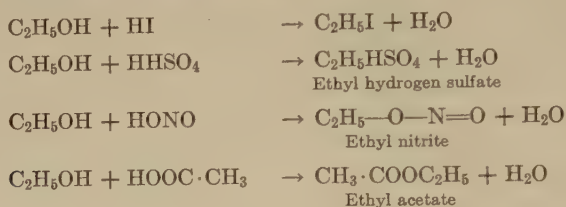
ESTERS

An **ester** is an inorganic or organic acid in which the acid hydrogen has been replaced by an R group (or a salt in which the metal is replaced by an R group):

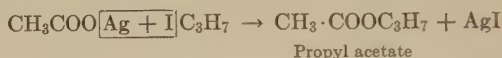


Esters are widely distributed in nature; they are responsible for the characteristic odors of many fruits, flavors, and flowers. Having very agreeable odors, they are used as flavoring materials and in perfumes. Since they are volatile, the esters have also been called "ethereal salts." Most of them are insoluble in water.

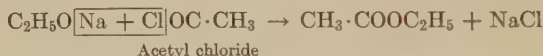
General Methods of Preparation. Esters are prepared: 1. By the interaction of an alcohol and an acid; e.g.,



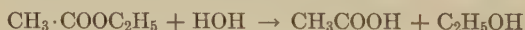
2. By the interaction of a salt of an acid with an organic halide; e.g.,



3. By the action of an acyl halide on an alcohol or an alkoxide; e.g.,

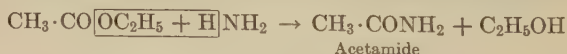


General Properties. The esters are neutral substances, insoluble in water. Though salts ionize, esters do not. Upon boiling with dilute acid or alkali, hydrolysis takes place:

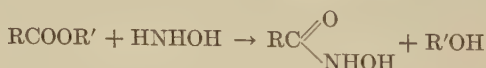


With alkali the reaction is known as **saponification**, since in the case of fats it yields soap as well as glycerol.

Ammonia converts esters to the corresponding amides; e.g.,

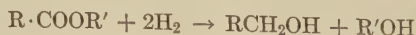


A similar reaction takes place with hydroxylamine:

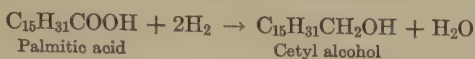


These hydroxamic acids form colored metallic salts (Fe^{+++}) which can be used to detect acids and their derivatives.

With hydrogen under pressure and a catalyst (Ni, Pt), an ester is reduced to a primary alcohol:

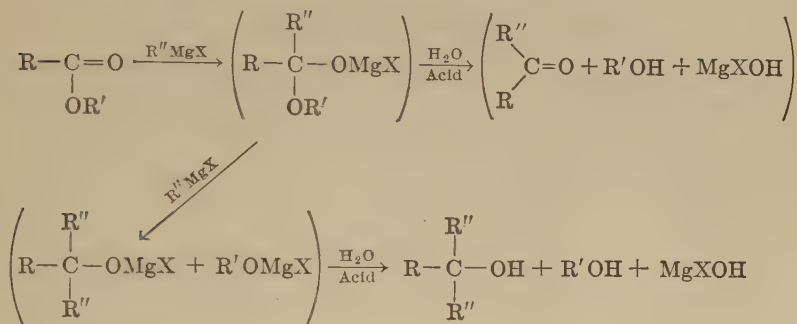


Under similar conditions, higher fatty acids (from fats) can be reduced to corresponding primary alcohols. For example,



This method is used to produce the higher alcohols from which sulfate detergents are made.

As carbonyl compounds, esters react with the *Grignard* reagent; little, if any, of the ketone which might be expected is formed, however. The principal reaction is one which involves two moles of magnesium compound to one of ester and yields, after hydrolysis of the addition complex, a tertiary alcohol:



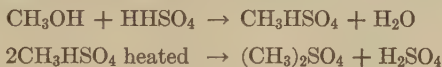
The product is the same as that which would be formed if the ketone were to react with the second mole of a Grignard reagent.

Esters of Inorganic Acids. The alkyl halides discussed in Chapter IV are esters of hydriodic, hydrobromic, and hydrochloric acids.

Ethyl nitrite, $\text{C}_2\text{H}_5\cdot\text{ONO}$, has an apple-like odor. Its alcoholic solution is the "sweet spirit of nitre." **Isoamyl nitrite**, $i\text{-C}_5\text{H}_{11}\cdot\text{ONO}$, is used in medicine as an antispasmodic and anodyne.

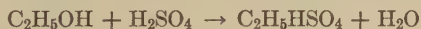
Ethyl nitrate, $\text{C}_2\text{H}_5\text{ONO}_2$, has a fruity odor. It is explosive.

Dimethyl sulfate, $(\text{CH}_3)_2\text{SO}_4$, may be prepared thus:



It finds use as a methylating agent (to introduce methyl groups into compounds). It is poisonous.

Ethyl sulfuric acid, $\text{C}_2\text{H}_5\text{HSO}_4$ (also called **ethyl hydrogen sulfate**), may be prepared by the action of concentrated sulfuric acid on ethyl alcohol at 100° :

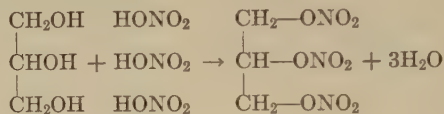


It may be recalled at this point that, when ethyl hydrogen sulfate is

heated to about 170° , we get ethylene, and, when it is treated with alcohol, it yields ether.

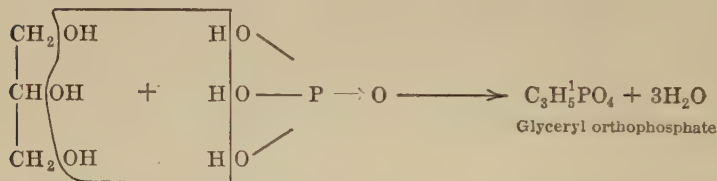
Diethyl sulfate, $(C_2H_5)_2SO_4$, is used as an ethylating agent. It has a peppermint-like odor. Unlike dimethyl sulfate, it is non-toxic. The sodium salts of higher alkyl acid sulfates (RCH_2OSO_2ONa) are useful detergents.

Glyceryl trinitrate, commonly, but erroneously, called **nitroglycerin**, is prepared by the action of nitric acid on glycerol (H_2SO_4 is used as a dehydrating agent):



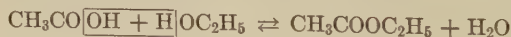
It is used in medicine as a circulatory depressant and is the active constituent of dynamite.

Glyceryl phosphate (ortho) is prepared in a similar manner:



RCN may be regarded as an ester of HCN . This type of compound will be treated later (p. 184).

Esters of Organic Acids. When an inorganic acid and a base react, a salt is immediately formed; when, however, an organic acid and an alcohol (in some respects the analog of the base) react, the ester is formed, but slowly:



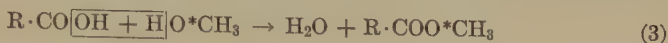
The formation of water by the action of acid and alcohol may be represented in one of two ways:



By using methyl alcohol containing heavy oxygen (O^* , atomic weight 18) and reacting it with acid, it has been possible to show that

¹ The C_3H_5 group, if trivalent, is the glyceryl group; if C_3H_5 is monovalent, it is the allyl group.

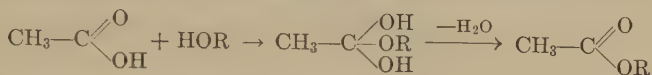
the water resulting from the reaction contains the ordinary oxygen (atomic weight 16), and *not* the isotopic form:



which proves that the oxygen in the water originates in the acid; and that, therefore, equation 3 and also equation 1 are correct.

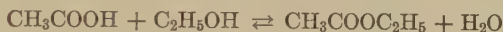
A rise in temperature or the use of a catalyst (H^+) increases the velocity of the reaction but does not appreciably change the yield of ester. The yield may be increased by the addition of a dehydrating agent, such as H_2SO_4 or HCl gas.

The mechanism for the formation of an ester may be illustrated thus:



Esterification. When an alcohol and an organic acid react, the reaction does not go to completion. In the formation of ethyl acetate from equimolecular quantities of alcohol and acid, no matter how long we wait, not more than 66 per cent is formed at room temperature (25°). Furthermore, if ethyl acetate is treated with water (hydrolysis) to get ethyl alcohol and acetic acid, not more than about one-third of the ethyl acetate will decompose, leaving about 66 per cent undecomposed. Obviously, we are dealing with a reversible-reaction mixture which, at equilibrium, contains 66 per cent of ethyl acetate.

If we apply the mass-action law to the reaction



then

$$\frac{[\text{CH}_3\text{COOC}_2\text{H}_5] \times [\text{H}_2\text{O}]}{[\text{CH}_3\text{COOH}] \times [\text{C}_2\text{H}_5\text{OH}]} = K$$

where [] represent concentrations in moles per liter and K is the equilibrium constant.

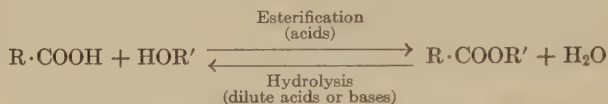
To determine K , we know from experiment that, when 1 mole of acetic acid and 1 mole of ethyl alcohol, a total of 2 moles, react, $\frac{2}{3}$ mole of ester and $\frac{2}{3}$ mole of water are formed. This means that $\frac{1}{3}$ mole each of acid and alcohol remain. Substituting these values in the equation,

$$\frac{\frac{2}{3} \times \frac{2}{3}}{\frac{1}{3} \times \frac{1}{3}} = 4$$

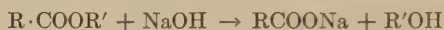
Thus K has a value of 4. Knowing now the value of K for an ester at a definite temperature, we can, of course, calculate the composition of an equilibrium mixture obtained by starting with definite amounts of acid and alcohol.

It can be shown, using the mass-law equation, that, by increasing the concentration of alcohol or of acetic acid, the yield of ester will be increased. The reaction can also be made to go more to the right (yield more ester) by removing one of the products formed (such as the water), wherever that is possible.

The extent of esterification of acetic acid with alcohol is dependent upon whether the alcohol is primary, secondary, or tertiary. More ester is produced with primary than with secondary alcohols, and more with secondary than with tertiary alcohols.



Saponification (alkaline hydrolysis) is an irreversible reaction:



Many esters are known. They are used extensively in artificial fruit essences, flavors, perfumes, extracts, etc. Only a few can be mentioned here.

Ethyl acetate, $\text{CH}_3 \cdot \text{COOC}_2\text{H}_5$, is used as a solvent for nitrocellulose, in the preparation of photographic films, and in resins and essences.

Isoamyl acetate, $\text{CH}_3 \cdot \text{COOC}_5\text{H}_{11}$, found in pear oil, is used as a solvent for guncotton and in the preparation of artificial banana oil or "bronzing" liquid.

Ethyl butyrate, $\text{C}_3\text{H}_7 \cdot \text{COOC}_2\text{H}_5$, occurs in pineapples.

Isoamyl isovalerate, $\text{C}_4\text{H}_9 \cdot \text{COOC}_5\text{H}_{11}$, is found in apples.

Octyl acetate, $\text{CH}_3 \cdot \text{COOC}_8\text{H}_{17}$, occurs in oranges.

Ethyl formate, $\text{H} \cdot \text{COOC}_2\text{H}_5$, is a constituent of artificial rum flavor.

Amyl butyrate, $\text{C}_3\text{H}_7 \cdot \text{COOC}_5\text{H}_{11}$, has an apricot flavor.

Vinyl acetate, $\text{CH}_3 \cdot \text{COOCH}=\text{CH}_2$, is used in the manufacture of synthetic resins. With vinyl chloride it forms some valuable copolymers of the "Vinylite" group, including "Vinyon," a textile fiber.

Saponification of polyvinyl acetate yields polyvinyl alcohol, which, unlike its monomer, is stable and even reacts with aldehydes to form polymeric acetals.

Glycol diacetate, $\text{CH}_3 \cdot \text{COOCH}_2$, is used as a solvent for cellulose

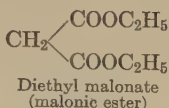
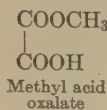
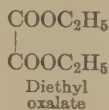


acetate and in cellulose nitrate lacquers.

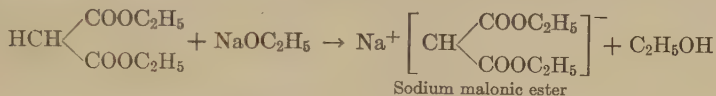
As a result of the development of the lacquer industry during the last few years, many of these esters are now finding extensive use.

Myricyl palmitate, $\text{C}_{15}\text{H}_{31} \cdot \text{COOC}_{30}\text{H}_{61}$, is present in beeswax.

Esters of methacrylic acid, $\text{CH}_2=\text{C}-\text{COOH}$, such as **methyl methacrylate**, $\text{CH}_2=\text{C}-\text{COOCH}_3$, etc., are polymerized into the so-called methacrylate resins. ("Lucite," etc.). The esters of dibasic acids are also well known; e.g.,

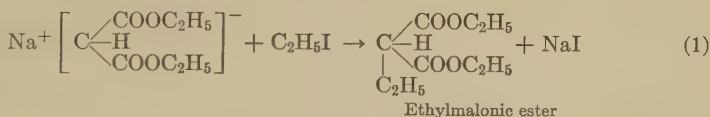


Esters of Dicarboxylic Acids. Malonic ester is used to synthesize homologs of malonic and acetic acids. When malonic ester is treated with sodium in absolute alcohol the following reaction takes place:

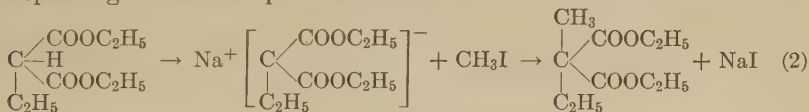


Diethyl malonate offers another example of the influence of negative groups upon the mobility of neighboring hydrogens. Here the methylene group is alpha to two COOC_2H_5 groups, and the hydrogens are easily removed by bases.

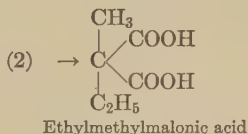
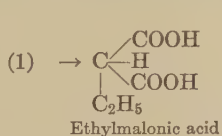
If an alkyl halide is now added, a derivative of malonic ester is obtained:



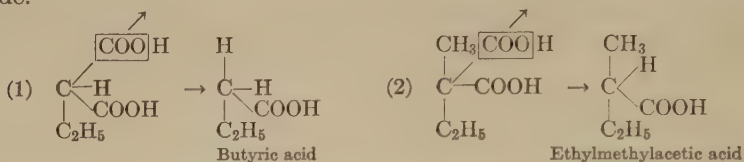
A second alkyl group (the same or a different one) may be introduced by repeating the above operation:



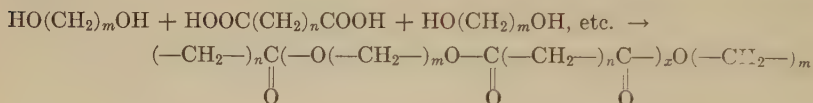
On hydrolysis with aqueous sodium hydroxide and subsequent acidification the following acids are formed:



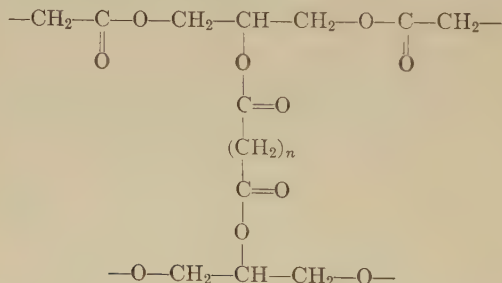
On heating, malonic acid and substituted malonic acids lose carbon dioxide.



The reaction of dicarboxylic acids with polyhydric alcohols does not yield the simple intermolecular esters which might be expected, but instead, high-molecular-weight linear "polyesters." These are apparently produced by the reaction of a different molecule of alcohol for each carboxylic function involved.



If glycerol is used, cross linkages are formed:



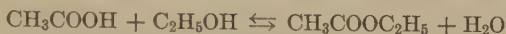
The condensation of glycerol with dibasic acids, such as phthalic acid (p. 298), and aliphatic acids is used to make "alkyd" resins. These polymers are formed by the elimination of a simple molecule, such as water, and they are known as "condensation polymers" in contradistinction to "addition polymers."

Animal and vegetable fats and oils are glyceryl esters. They will be taken up in detail in the next chapter.

QUESTIONS

1. Write structural formulas for (a) cupric acetate; (b) calcium malonate; (c) sodium acid succinate; (d) sodium formate; (e) ferric succinate; (f) lead oleate; (g) magnesium butyrate; (h) ethyl acetate; (i) ethyl nitrite; (j) ethyl nitrate; (k) dimethyl sulfate; (l) triethyl phosphate; (m) di-*n*-butyl sulfate; (n) glyceryl nitrate; (o) ethylene glycol acetate; (p) ethylidene acetate; (q) isobutyl iodide; (r) methyl ethyl succinate; (s) ethylmalonic acid; (t) ethyl acid malonate; (u) sodium malonic ester; (v) vinyl acetate; (w) ethyl butyrate.

2. Construct the formulas and give the names of three esters represented by the formula $C_6H_{10}O_2$.
3. Show, by means of equations, how acids of the following structures could be prepared by the use of the malonic ester synthesis: (a) C_3H_7COOH ; (b) $C_2H_5 \cdot CH(COOH)_2$; (c) $(C_2H_5)(CH_3)C(COOH)_2$; (d) $(CH_3)_2CH \cdot COOH$.
4. Indicate what is meant by the terms (a) ester; (b) salt; (c) soap; (d) esterification; (e) saponification; (f) hydrolysis; (g) acid salt; (h) "salting out."
5. Eight milliliters of acetone (sp. gr. 0.79) was obtained as the result of distilling 60 grams of calcium acetate; what percentage of the theoretical yield was obtained?
6. The equilibrium constant has a value of 4 (at $25^\circ C$) for the reaction:



Calculate the weight of ethyl acetate present at equilibrium when one mole of acetic acid is treated with (a) two moles of ethyl alcohol; (b) ten moles of ethyl alcohol.

7. Describe the following syntheses:

(a) sodium propionate	from ethyl cyanide
(b) methane	" sodium acetate
(c) acetaldehyde	" calcium acetate
(d) acetone	" calcium acetate
(e) ethyl acetate	" acetyl chloride
(f) <i>n</i> -propyl butyrate	" potassium butyrate
(g) methylethylmalonic acid	" malonic acid
(h) methyl iodide	" methyl butyrate
(i) diethyl malonate	" naturally occurring materials
(j) ethyl acid succinate	" sodium acid succinate
(k) dimethyl sulfate	" methanol
(l) ethylene glycol acetate	" ethylene chloride
(m) ethyl hydrogen sulfate	" ethanol
(n) diethyl methyl carbinol	" ethyl acetate
(o) sodium lauryl sulfate	" glyceryl trilaurate

8. Discuss the new types of soaps or detergents.
9. Discuss the mechanism of ester formation from an alcohol and an acid.
10. (a) What is the structure of methacrylic acid? (b) Discuss the commercial application of its alkyl esters.
11. How much alcohol and ester will there be at equilibrium at 25° in a mixture of 20 grams of ethyl acetate and 30 grams of water?
12. (a) Explain the cleansing action of soap. (b) Show by means of structural formulas the similarities between soap and the sulfate detergents. (c) What are the advantages of the new detergents?
13. How can we account in terms of resonance for the ease of reduction of esters as compared with free acids?

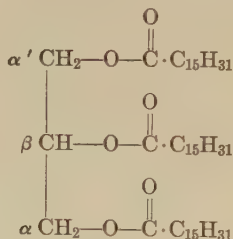
CHAPTER X

FATS AND OILS, WAXES, AND SOME LIPIDS

FATS AND OILS

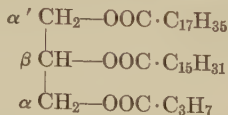
Fats and oils are glyceryl esters of fatty acids (usually of high molecular weight). There is no essential difference between fats and oils. The fats are solid at ordinary temperatures, whereas the oils are liquid.

An example of one of these substances is glyceryl palmitate (tripalmitin).



Glyceryl esters of stearic ($\text{C}_{17}\text{H}_{35}\text{COOH}$), palmitic ($\text{C}_{15}\text{H}_{31}\text{COOH}$), and oleic ($\text{C}_{17}\text{H}_{33}\text{COOH}$) acids constitute the main bulk of the fats in food and in body fat.¹

If the three acid radicals in a fat molecule are the same, the glyceride is simple, e.g., tripalmitin. A glyceride containing radicals of two or three different fatty acids is known as a mixed glyceride, e.g.,



Stearin, $\text{C}_3\text{H}_5(\text{OOC} \cdot \text{C}_{17}\text{H}_{35})_3$, and **palmitin**, $\text{C}_3\text{H}_5(\text{OOC} \cdot \text{C}_{15}\text{H}_{31})_3$, are solids; **olein**, $\text{C}_3\text{H}_5(\text{OOC} \cdot \text{C}_{17}\text{H}_{33})_3$, is a liquid. The consistency of a fat or oil depends on the amount of solid or liquid esters present.

Oleomargarine consists mainly of refined lard, "oleo oil" (the soft part of beef fat), and cottonseed oil, often mixed with a small amount of butter and churned with milk or cream.

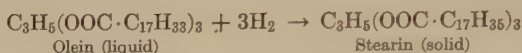
¹ Such unsaturated acids as linoleic and linolenic (p. 105), which occur in fats in small quantities, are necessary for proper nutrition.

IMPORTANT FATS AND OILS

Fat or Oil	Contains the Glyceryl Ester of	Source of Fat or Oil
Almond oil	Oleic, palmitic, linoleic acids, etc.	Bitter or sweet almonds
Butterfat	Butyric, caproic, capric, palmitic, stearic, oleic acids, etc.	Cow's milk
Cacao butter	Palmitic, oleic, stearic, myristic acids, etc.	Seeds of cocoa nibs
Castor oil	Ricinoleic, stearic, oleic acids, etc.	Seeds of castor beans
Coconut oil	Caproic, caprylic, capric, lauric acids, etc.	Seeds of <i>Cocos nucifera</i> , kernel of nuts
Cod-liver oil	Oleic, myristic, palmitic, stearic acids, and cholesterol, etc.	Livers of codfish
Cottonseed oil	Oleic, stearic, palmitic, linoleic acids, etc.	Seeds of the cotton plant
Hemp oil	Isolinolenic, oleic acids, etc.	Seeds of hemp
Human fat	Stearic, palmitic, oleic, butyric, caproic acids, etc.	Human beings
Lard	Stearic, palmitic, oleic, linoleic acids, etc.	Body fat of swine
Linseed oil	Linoleic, linolenic, oleic, palmitic, myristic acids, etc.	Seeds of flax
Maize oil	Arachidic, stearic, palmitic, oleic acids, etc.	Seed germs of corn oil
Menhaden oil	Palmitic, myristic, oleic, stearic, and other unsaturated acids, etc.	Bodies of menhaden fish
Mustard oil	Erucic, arachidic, stearic, oleic acids, etc.	Seeds of mustard
Neatsfoot oil	Palmitic, stearic, oleic acids, etc.	Hoofs of cattle
Olive oil	Linoleic, oleic, arachidic acids, etc.	Fruit of olive tree
Palm oil	Palmitic, lauric, oleic acids, etc.	Palm seed
Peanut oil	Arachidic, linoleic, hypogaeic, palmitic acids, etc.	Peanuts
Poppy oil	Linoleic, isolinolenic, palmitic, stearic acids, etc.	Poppy seeds
Rape oil	Erucic, arachidic, stearic acids, etc.	Rape seeds
Soybean oil	Oleic, linoleic, linolenic acids, etc.	Soybeans
Sperm oil	Oleic, palmitic acids, waxes, etc.	Head and blubber of sperm whale
Tallow	Stearic, palmitic, oleic acids, etc.	Fat of ox or sheep
Whale oil	Linoleic, isolinolenic acids, etc.	Blubber of whales

Hydrogenation of Oils. Liquid fatty oils can be converted to fats of almost any desired degree of consistency by means of hydrogenation. The unsaturated liquid oils unite directly with hydrogen in presence of

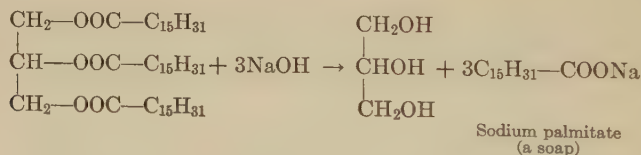
catalysts (nickel being used on a commercial scale) to form saturated compounds.



Stearin has greater commercial value than olein. The "hardened fats" now find extensive use in the preparation of lard substitutes, in the manufacture of soap, etc. "Hardened" cottonseed oil, peanut oil, and other edible oils have largely replaced lard compounds. "Crisco," "Spry," and "Vegetol" are examples of "hardened" (or hydrogenated) vegetable oils. Fish oils are hydrogenated, much of the fishy odor being thereby removed; the product is used in the manufacture of soaps.

Crude fats and oils range from yellow to red in color. The refined products are generally yellow to colorless. Sometimes vegetable oils are green, owing to the presence of chlorophyll (the green coloring matter of plants). Fats and oils are insoluble in water but readily soluble in ether, benzene, chloroform, etc. The rancidity of a fat (as in butterfat) is mainly due to hydrolysis (bacterial decomposition, or otherwise) and oxidation yielding the free fatty acids. Butter in this way produces butyric acid, which has a disagreeable odor.

Properties. Fats can be hydrolyzed or saponified. When the glyceryl esters of stearic, palmitic, or oleic acids are saponified with NaOH or KOH, soaps are formed:



This is the reaction employed in the manufacture of soap. It also explains the hydrolysis of fats in the small intestine by the enzyme (lipase) which is formed in the pancreas.

A number of analytical constants used for identifying fats are:

1. *Saponification Number.* This represents the number of milligrams of KOH needed to saponify 1 gram of fat or oil. In a general way, this number varies inversely with the molecular weight of the fat. For example,

	M.W.	SAPONIFICATION NO.
Tributyrin	302.2	557.0
Tripalmitin	806.8	208.6
Tristearin	890.9	188.9
Triolein	884.8	190.2

2. *Iodine Number*. This is the number of grams of iodine absorbed by 100 grams of fat. The iodine number depends upon the extent of unsaturation of the fat. For example,

	IODINE NO.
Butter	26-50
Lard	46-70
Tallow	35-46
Olive oil	79-88
Linseed oil	173-201
Cottonseed oil	108-110
Coconut oil	8-10

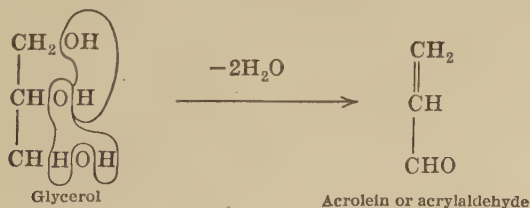
I_2 does not add to double bonds; but such reagents as ICl and IBr produce diiodo compounds in these cases.

3. *Reichert-Meissl Number*. This is the number of milliliters of 0.1 *N* alkali required to neutralize the soluble volatile fatty acids from 5 grams of fat. Among fats, butter has a high Reichert-Meissl number (26-33).

4. *Acetyl Number*. This is the number of milligrams of KOH required to neutralize the acetic acid resulting from the hydrolysis of 1 gram of the acetylated fat. This reaction depends upon the presence of hydroxyl groups. Castor oil, which contains the unsaturated fatty acid ricinoleic acid, has a high acetyl number (142-150). The common fats, containing much smaller quantities of hydroxy fatty acids, have much smaller numbers (2.5-20).

In the body, the fats are first hydrolyzed into fatty acids and glycerol. The fatty acids and glycerol are absorbed as such through the lining of the small intestine, where they are resynthesized into fat, most of which passes into the lymphatic system, and finally finds its way into the blood stream. Some of the fat is oxidized in the cells to CO_2 and water, and some of it is deposited in the adipose and other tissues.

The fats and oils, when strongly heated, either alone, or with a dehydrating agent like $KHSO_4$, develop a penetrating odor, owing to the formation of acrolein. This acrolein is really derived from the glycerol part of the molecule:



WAXES

Waxes, like fats, are esters, but, instead of containing the glyceryl group, they are the esters of high-molecular-weight alcohols, such as cetyl alcohol, $C_{16}H_{33}OH$, carnaubyl alcohol, $C_{24}H_{49}OH$, myricyl alcohol, $C_{30}H_{61}OH$, with high-molecular-weight fatty acids. An example of a wax is myricyl palmitate, $C_{15}H_{31} \cdot COOC_{30}H_{61}$, present in beeswax.

Among vegetable waxes we have carnauba wax, and among animal waxes we have wool wax or lanolin, beeswax, spermaceti, and Chinese insect wax.

Waxes, like fats, are soluble in ether, benzene, chloroform, and carbon tetrachloride. Since they do not contain the glyceryl radical, they do not yield acrolein when heated. The waxes do not become rancid like fats, and they are less easily hydrolyzed.

Carnauba wax is derived from a species of palm; it is used in varnish, for candlemaking, and for adulterating beeswax. Lanolin, obtained from wool grease, is used in pharmacy as a basis for salves, ointments, and emulsions. Beeswax, derived from the honeycomb of bees, is used in candlemaking and in pharmacy. Spermaceti, found in the head of the sperm whale, finds uses in candlemaking, in pharmacy, and in confectionery. Chinese wax, secreted by an insect, is also used in candlemaking, in medicine, and as a furniture polish.

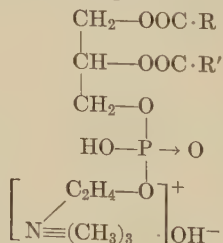
SOME LIPIDS

The lipids include both fats and waxes. In addition, they also include:

1. Phospholipids: fats which contain phosphoric acid and nitrogenous groups (lecithin, cephalin, sphingomyelin).
2. Cerebrosides, containing fatty acid, some sugar, and a nitrogenous substance (phrenosin, kerasin).
3. Sterols: hydrogenated phenanthrene derivatives (cholesterol, ergosterol, etc.).

These lipids are found in the animal and plant kingdoms and are soluble, in varying degree, in ether and in other fat solvents.

Lecithin is a combination of glycerol, fatty acid, phosphoric acid, and choline, and its structure may be represented as:



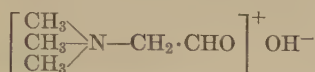
R and R' represent groups present in acids. As in fats, R and R' may be the same or different.

In a crude form, lecithin may be obtained from egg yolk by extracting with ether and precipitating with acetone. In the industries many thousands of pounds of lecithin, obtained from soybean, are used as an emulsifier and in the manufacture of candies, chocolate, cocoa, margarine, medicines, and in the dyeing of textiles.

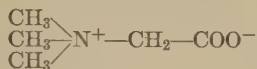
Choline,



or trimethyl- β -hydroxyethyl ammonium hydroxide, is related to **muscarine**,

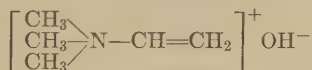


which is the poisonous constituent of the deadly toadstool, and to **betaine**, an inner salt:

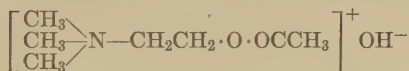


Betaine is a non-toxic plant product.

Neurine, a product of putrefaction, is vinyl trimethyl ammonium hydroxide:



Acetylcholine.

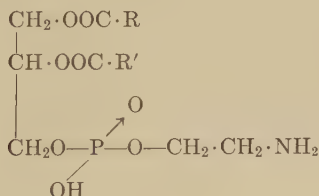


is liberated upon the stimulation of nerve endings in voluntary muscle.

Cephalin is similar to lecithin in that it contains glycerol, fatty acids, and phosphoric acid, but, in place of the base choline, it contains aminoethyl alcohol, $\text{CH}_2 \cdot \text{CH}_2\text{OH}$. Its constitution may be represented



as



Unlike lecithin, cephalin is insoluble in alcohol. (Cephalin is sometimes written "kephalin.")

Sphingomyelin is a complex combination of phosphoric acid, choline, a base, sphingosine, $C_{17}H_{32}(OH)NH_2$, and an acid, lignoceric acid, $C_{23}H_{47}\cdot COOH$.

Phrenosin is a combination of cerebronic acid (the hydroxy acid of lignoceric), galactose, and sphingosine.

Cerasin, like phrenosin, yields, when hydrolyzed, galactose and sphingosine, but in the place of cerebronic acid, it gives lignoceric acid.

Cholesterol, $C_{27}H_{45}OH$, is an unsaturated secondary alcohol. It is widely distributed in animal tissues, particularly in egg yolk and nervous tissue. Isomers, **phytosterols**, are found in the vegetable kingdom. Lanolin, the fatty matter obtained from sheep's wool, is an ester of cholesterol. This alcohol is also present in bile and in blood, and the bile salts are derivatives of cholesterol. (See p. 397.)

QUESTIONS

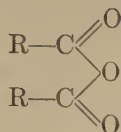
1. Making use of glycerol and only the three acids, oleic, palmitic, and stearic, how many different triglycerides could theoretically be produced? Name them.
2. Write structural formulas for: (a) methyl stearate; (b) tributyrin; (c) neurine; (d) choline; (e) muscarine; (f) betaine; (g) lecithin.
3. Describe the following preparations:

(a) sodium oleate	from triolein
(b) glyceryl trinitrate	" tripalmitin
(c) stearin	" triolein
(d) zinc stearate	" tristearin
(e) acrolein	" tributyrin
(f) ethyl palmitate	" tripalmitin
(g) butyric acid	" butter
4. Calculate the saponification and iodine numbers of tributyrin, triolein, and tristearin.
5. What volume of hydrogen at $15^{\circ}C$ and 755 mm would be necessary to hydrogenate two moles of a mixed glyceride of palmitic and oleic acids (1 palmitic : 2 oleic)?

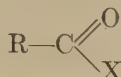
CHAPTER XI

ACID ANHYDRIDES, ACYL HALIDES, AND ACID AMIDES

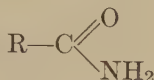
The type formula for an acid anhydride is



The type formula for an acyl halide is

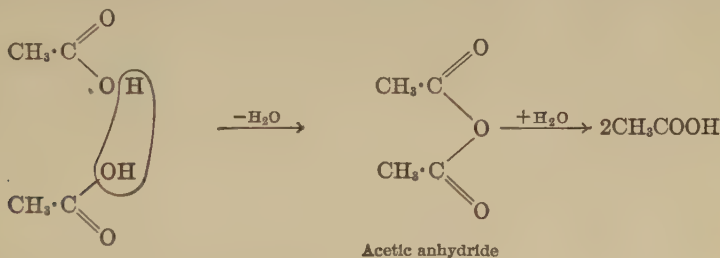


The type formula for an acid amide is



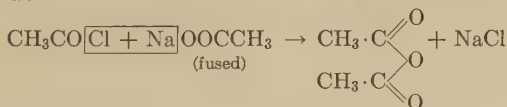
ACID ANHYDRIDES

Acid anhydrides are similar in many respects to inorganic acid anhydrides. Sulfur trioxide, for example, is the acid anhydride of sulfuric acid, for $\text{SO}_3 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{SO}_4$. Similarly, acetic (acid) anhydride is the anhydride of acetic acid, for



(Ketene, p. 97, is the anhydride of one mole of acetic acid.)

Acid anhydrides are generally prepared by heating an acyl halide and a salt of an acid:

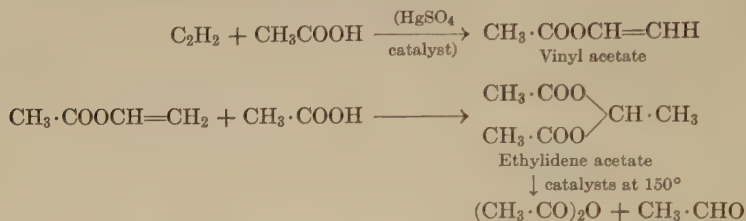


The action of a dehydrating agent like P_2O_5 on the acid yields very little anhydride, and the method is of little practical value.

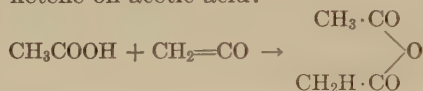
Acetic anhydride is the most important member of the series, and a summary of its properties presents the general properties of the anhy-

drides. (Formic anhydride is not known.) Commercially, acetic anhydride is made by:

1. Decomposing ethylidene acetate:



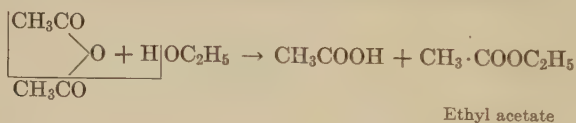
2. The action of ketene on acetic acid:



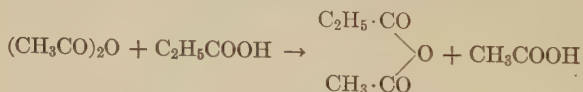
In addition to these methods of synthesis, acetic anhydride is also made industrially by dehydration of acetic acid with sulfur chloride, S_2Cl_2 .

It has already been mentioned that acetic anhydride reacts with water to form acetic acid. Very often, therefore, acetic anhydride is used with glacial acetic acid to ensure complete freedom from water in reaction mixtures.

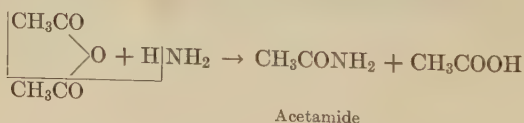
With an alcohol, a mixture of acid and ester is formed:



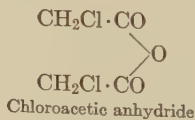
With another acid, a mixed anhydride is obtained:



With ammonia, the corresponding amide is formed:

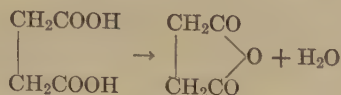


Chlorine and bromine yield substituted anhydrides; e.g.,

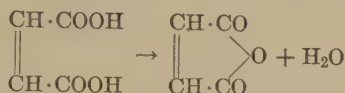


Acetic anhydride is a liquid with a pungent, suffocating odor. It is soluble in alcohol, chloroform, and ether. It finds extensive use as a means of introducing the CH_3CO (acetyl) group into compounds (for example, cellulose acetate).

Succinic anhydride may be obtained by heating succinic acid:



Similarly **maleic anhydride** may be obtained from maleic acid:

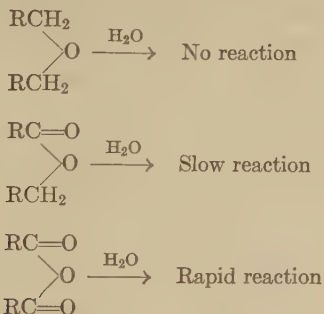


The fact that maleic anhydride is unsaturated makes possible a number of important reactions. With substances containing a conjugated double bond system, such as abietic acid (p. 361), and a number of terpenes (p. 358), synthetic resins may be obtained.

The anhydrides, in general, are liquids and boil at higher temperatures than their corresponding acids. They form esters even more readily than the acids. Many of these esters, particularly the acetates, are important, for example, the esters of cellulose (p. 208), phenols (p. 278), sugars (p. 193), and vegetable oils. Some of the cellulose esters are known as acetate rayon, safety photographic film, and cellulose acetate plastics and lacquers.

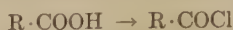
The anhydrides are also used in the manufacture of dyestuffs, resins, aspirin, etc.

The series ether, ester, acid anhydride provides an interesting parallel between structure and reactivity, the influence of increasing negativity on interatomic bonds being very clear in such reactions as, for instance, that with water.



ACYL HALIDES

Acyl halides, $\text{R}-\text{C} \begin{smallmatrix} \nearrow \text{O} \\ \searrow \text{X} \end{smallmatrix}$, may be regarded as acids in which the OH of the COOH group is replaced by a halogen:



The chlorides are common, but few of the corresponding iodides and bromides are known, and they are used only infrequently.

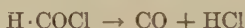
Nomenclature. The group $\text{R}-\text{C} \begin{smallmatrix} \nearrow \text{O} \\ \searrow \end{smallmatrix}$ is known as an "acyl" group.

The group $\text{CH}_3-\text{C} \begin{smallmatrix} \nearrow \text{O} \\ \searrow \end{smallmatrix}$ is known as the "acetyl" group.

The group $\text{C}_2\text{H}_5-\text{C} \begin{smallmatrix} \nearrow \text{O} \\ \searrow \end{smallmatrix}$ is known as the "propionyl" group.

Therefore, in naming the acyl halide, we need merely change the -ic (last two letters) of the acid to -yl.

Formyl chloride is not known. When the attempt is made to prepare it, it breaks down into CO and HCl,



a mixture which in many reactions acts like formyl chloride.

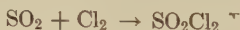
Acetyl chloride finds extensive use in organic syntheses, and its preparation and properties will, therefore, be considered.

Preparation. 1. Acetyl chloride can be made by the action of phosphorus pentachloride, phosphorus trichloride, or phosphorus oxychloride on acetic acid or sodium acetate:

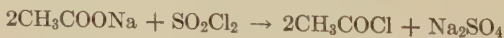


These reactions are analogous to those of $\text{ROH} \rightarrow \text{RCl}$.

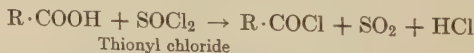
2. The commercial method of obtaining the chloride is to heat sodium acetate and to pass sulfur dioxide and chlorine over it. The sulfur dioxide and chlorine combine to form sulfuryl chloride:



which then reacts with the sodium acetate:

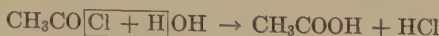


3.



This is a very useful laboratory preparation of acyl chlorides, especially since the by-products are gaseous and are easily removed.

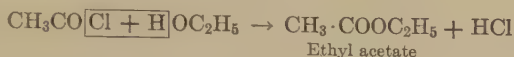
Properties. Acetyl chloride is used extensively to introduce the $\text{CH}_3-\text{C} \begin{smallmatrix} \diagup \text{O} \\ \diagdown \end{smallmatrix}$ (acetyl) group into organic compounds. It is a very reactive substance. The moisture of the atmosphere very readily converts it to acetic acid:



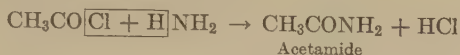
Acetyl chloride reacts with sodium acetate to form acetic anhydride:



and with ethyl alcohol to form an ester:



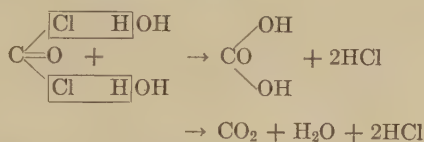
and with ammonia to form an amide:



If the OH groups in carbonic acid, $\text{C} \begin{smallmatrix} \diagup \text{OH} \\ \diagdown \text{OH} \end{smallmatrix}$ are replaced by Cl, we get $\text{C} \begin{smallmatrix} \diagup \text{Cl} \\ \diagdown \text{Cl} \end{smallmatrix}$ (chloroformyl or carbonyl chloride), which is commonly known as

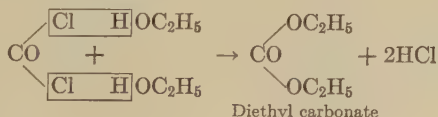
phosgene. This substance is a colorless, suffocating gas. Owing to its poisonous character, the comparative ease with which it can be liquefied and prepared (by passing chlorine and carbon monoxide over charcoal), phosgene was used very extensively in World War I. It was loaded in shells and bombs and exploded when the shell struck ground. Phosgene is also used in the manufacture of dyes.

Water decomposes phosgene as follows:

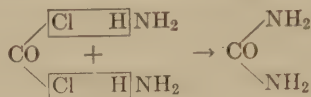


The poisonous effects of phosgene are said to be due to the liberation of a high concentration of HCl gas.

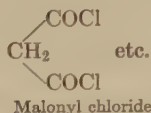
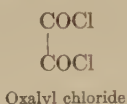
Ethyl alcohol forms an ester:



Ammonia transforms phosgene into urea (or carbamide):



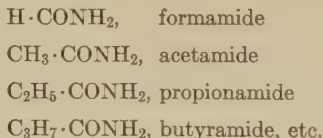
Other acyl halides are:



ACID AMIDES

Acid amides, $\text{R}-\text{C} \begin{array}{l} \nearrow \text{O} \\ \searrow \text{NH}_2 \end{array}$, may be looked upon as acids in which the OH group is replaced by NH_2 . They may also be regarded as derived from ammonia, NH_3 , in which one of the hydrogen atoms is replaced by the RCO (acyl) group. The $-\text{NH}_2$ group when attached to an acyl group is known as the "amido" group. If the $-\text{NH}_2$ group is attached to an alkyl group, it is known as the "amino" group.

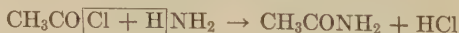
The nomenclature of amides is based on the names of the corresponding acids (amides of acids); e.g.,



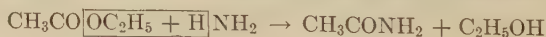
With the exception of formamide, which is a liquid, the amides are solids.

Acetamide can be taken as a type. It is prepared by:

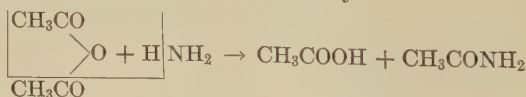
1. The action of ammonia on acetyl chloride:



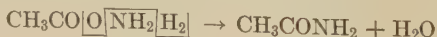
2. The action of ammonia on methyl and ethyl acetates:



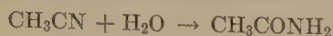
3. The action of ammonia on acetic anhydride:



4. The dehydration of ammonium acetate (by heating in a sealed tube or with glacial acetic acid):



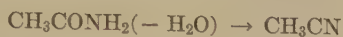
5. The partial hydrolysis of methyl cyanide:



Properties. Acetamide is transformed into ammonium acetate when boiled with acids or bases (compare with reaction 4 above):

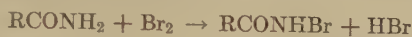


and when dehydrated forms methyl cyanide (compare with reaction 5 above):



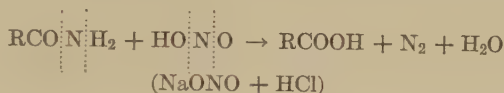
Formamide and acetamide possess solvent properties for both inorganic and organic compounds, owing to the polar functional groups; they are actually ionizing solvents.

When an amide is treated with a halogen in alkaline solution the following reactions take place:



This is a method by which the CO group can be eliminated from an amide, so that RCONH_2 becomes RNH_2 (amine) (*Hofmann reaction*).

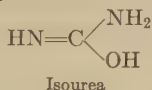
Nitrous acid reacts with the amido group to yield the carboxylic acid and nitrogen:



UREA

Urea, or carbamide, $\begin{array}{c} \text{NH}_2 \\ \diagup \\ \text{CO} \\ \diagdown \\ \text{NH}_2 \end{array}$, may be considered the diamino deriva-

tive of carbonic acid, $\begin{array}{c} \text{OH} \\ \diagup \\ \text{CO} \\ \diagdown \\ \text{OH} \end{array}$. Its imide formula is



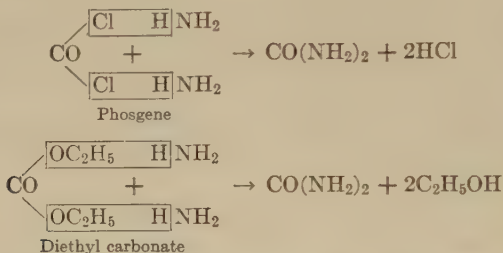
Urea is a substance of great biological importance, since it is the chief end product resulting from the changes that proteins undergo in the body. The amount of urea in the urine is directly proportional to the amount of protein present in the food which is eaten.

Preparation. 1. By heating ammonium cyanate a molecular rearrangement occurs:



This method was discovered by *Wöhler* in 1828. The student will recall that *Wöhler's* preparation is one of the earliest recorded instances of the laboratory preparation of an "organic" substance.

2. Urea, the amide of carbonic acid, may be prepared from the chloride or esters of that acid:



3. Another process, important industrially, depends upon the interaction of liquid NH_3 and liquid CO_2 in an autoclave:



This synthetic urea is now used extensively as a fertilizer.

Properties. Urea is easily hydrolyzed, yielding carbon dioxide and ammonia. These same products are also obtained when the enzyme *urease* (found in the soybean, etc.) is allowed to act on urea. (Incidentally, a good method for the determination of urea is based on its reaction with urease.) Nitrous acid liberates nitrogen, etc.:



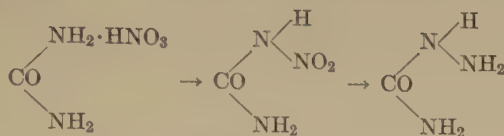
So does sodium hypobromite:



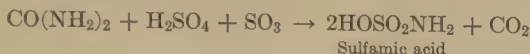
For a long time this method was used to determine urea. The nitrogen evolved was measured, and from it the amount of urea in the sample was calculated. The determination at best is only approximate, for the errors involved are high. The method has been largely replaced by the urease method.

Urea combines very readily with nitric and oxalic acids to form urea nitrate, $\text{CO}(\text{NH}_2)_2\cdot\text{HNO}_3$, and urea oxalate, $[\text{CO}(\text{NH}_2)_2]_2\cdot(\text{COOH})_2$, respectively. Only one NH_2 group of the urea molecule combines with the acid. These salts crystallize very readily and are often used for identifying urea.

Heating converts the nitrate to nitrourea which, by reduction, yields semicarbazide.

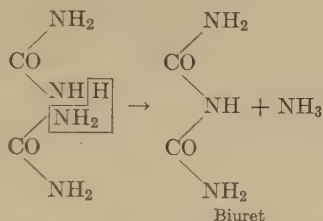


Treatment of urea with fuming sulfuric acid yields sulfamic acid, a very useful strong inorganic acid, which, being a solid, can be easily purified by crystallization.



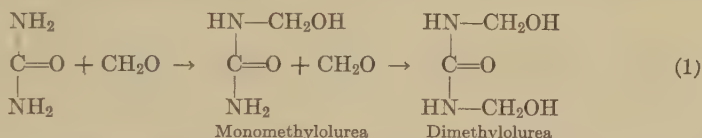
Its salts are used in flame-proofing, weed-killing, and electroplating.

When urea is heated, two molecules condense to form a substance known as **biuret**:

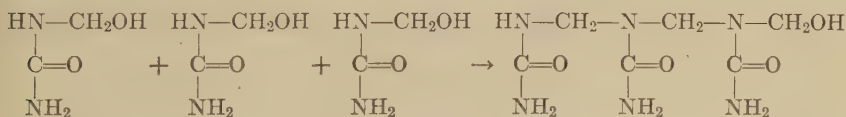


When a drop of dilute copper sulfate and fairly concentrated alkali are added to biuret, a violet color is formed. This is known as the "biuret reaction." All proteins give the biuret reaction—a reason for assuming that the protein molecule has, among other things, a "biuret" configuration.

In the presence of alkaline condensing agents, urea and formaldehyde combine to form methylolureas:



The methylolureas may then undergo condensation to form substances of higher molecular weight. Several reactions such as the following are possible:

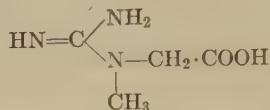


These methylolureas when impregnated into wood endow it with increased strength and resistance.

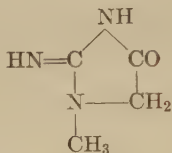
Urea combines with formaldehyde to form synthetic resins such as "Plaskon," which may be of similar structure.

Guanidine, $\text{HN}=\text{C} \begin{smallmatrix} \text{NH}_2 \\ \text{NH}_2 \end{smallmatrix}$, is related to urea.

Creatine,



or methylguanidinoacetic acid, is a constituent of muscle; and its anhydride, **creatinine**,



is a normal constituent of urine.

A number of derivatives of urea, such as urethane, $\text{C} \begin{smallmatrix} \text{NH}_2 \\ \text{=O} \\ \text{OC}_2\text{H}_5 \end{smallmatrix}$, or ethyl

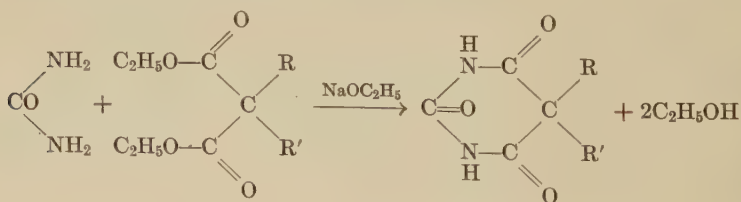
carbamate $\left(\text{CO} \begin{smallmatrix} \text{OH} \\ \text{NH}_2 \end{smallmatrix} \right.$ is carbamic acid); **barbital**, $\text{C} \begin{smallmatrix} \text{NH}-\text{C}=\text{O} \\ \text{=O} \\ \text{NH}-\text{C}=\text{O} \end{smallmatrix} \begin{smallmatrix} \text{C} \\ \text{C} \end{smallmatrix} \begin{smallmatrix} \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5 \end{smallmatrix}$,

or diethyl malonyl urea; **luminal** or **phenobarbital**, $\text{C} \begin{smallmatrix} \text{NH}-\text{C}=\text{O} \\ \text{=O} \\ \text{NH}-\text{C}=\text{O} \end{smallmatrix} \begin{smallmatrix} \text{C} \\ \text{C} \end{smallmatrix} \begin{smallmatrix} \text{C}_2\text{H}_5 \\ \text{C}_6\text{H}_5 \end{smallmatrix}$,

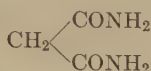
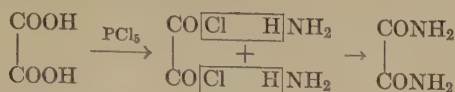
or phenyl ethyl malonyl urea; and **amytal**, $\text{C} \begin{smallmatrix} \text{NH}-\text{C}=\text{O} \\ \text{=O} \\ \text{NH}-\text{C}=\text{O} \end{smallmatrix} \begin{smallmatrix} \text{C} \\ \text{C} \end{smallmatrix} \begin{smallmatrix} \text{C}_5\text{H}_{11} \\ \text{C}_2\text{H}_5 \end{smallmatrix}$, or

isoamyl ethyl malonyl urea, are used extensively as hypnotics.

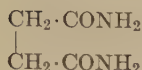
These important cyclic ureides are made by the condensation of urea with the appropriate substituted malonic esters:



Oxamide, $\begin{array}{c} \text{CONH}_2 \\ | \\ \text{CONH}_2 \end{array}$, is formed as follows:

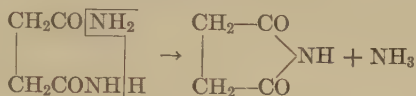


is malonamide,



is succinamide.

When succinamide is heated, succinimide is obtained, the $>\text{NH}$ group being known as the imido group:



The hydrogen of an atom alpha to a negative group (in this case alpha to *two* carbonyl groups) is unusually reactive (compare aldehydes, carboxylic acids, and malonic ester). This hydrogen in imides is replaceable by active metals like Na or K:



QUESTIONS

- Write structural formulas for the following: (a) acetic anhydride; (b) succinic anhydride; (c) maleic anhydride; (d) propionyl chloride; (e) oxalyl chloride; (f) phosgene; (g) urea; (h) propionamide; (i) biuret; (j) barbital; (k) succinimide; (l) chloroacetyl chloride; (m) malonamide; (n) chloroacetamide; (o) acetchloroamide.
- Describe the following syntheses:

(a) butyryl chloride	from ethyl butyrate
(b) propionic acid	" propionyl chloride
(c) acetamide	" acetyl chloride
(d) carbamide	" ethyl carbonate
(e) acetic acid	" acetamide
(f) butyramide	" methyl butyrate
(g) urea	" ammonium cyanate
(h) succinimide	" succinic acid

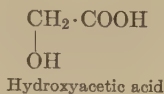
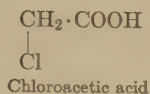
(i) oxamide	from cyanogen
(j) ethyl alcohol	" propionic acid
(k) acetic anhydride	" vinyl acetate
(l) ethanol	" methanol
(m) methanol	" ethanol
(n) acetamide	" methyl cyanide
(o) acetic-butyric anhydride	" ethanol

3. Guanidine is a strong base (the guanidinium ion is comparatively stable). Show how this may be explained in terms of resonance. (Compare the symmetry of the ion and of the free base.)

CHAPTER XII

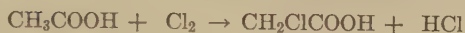
HALOGEN-SUBSTITUTED ACIDS AND HYDROXY ACIDS

These are acids in which one or more of the hydrogen atoms in the group attached to the COOH group is replaced by halogen or OH. For example, $\text{CH}_3\cdot\text{COOH}$, acetic acid, gives rise to



HALOGEN-SUBSTITUTED ACIDS

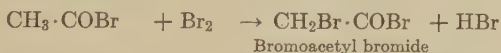
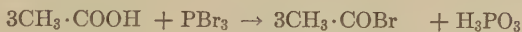
Preparation. The action of chlorine on acetic acid, for instance, yields chloro acids:



The number of hydrogen atoms replaced by chlorine atoms depends upon the amount of chlorine used and upon the temperature and the time of the reaction. These reactions are carried out in the presence of sunlight and "carriers"—catalysts—such as iodine or sulfur.

Analogous compounds may be formed by substituting bromine for chlorine, but here the reaction proceeds only under pressure and at higher temperatures. Iodine does not react. (In order to make such a substance as iodoacetic acid, we allow potassium iodide to react with chloroacetic acid: $\text{CH}_2\text{Cl}\cdot\text{COOH} + \text{KI} \rightarrow \text{CH}_2\text{I}\cdot\text{COOH} + \text{KCl}$.)

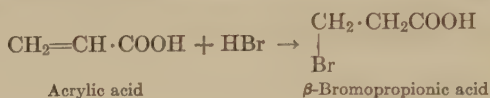
Better yields are obtained by the use of P and the halogen in the following way:



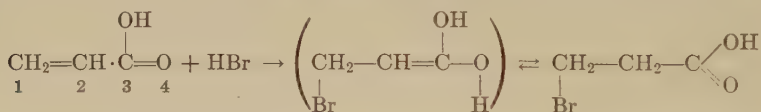
Acyl halides are much more easily hydrolyzed than alkyl halides, so that halogen acids can be obtained by treating haloacyl halides with water.

Direct halogenation always replaces the hydrogen attached to the α -carbon (which is the most labile, as we know).

β -Halogenated acids may be obtained in the following way:

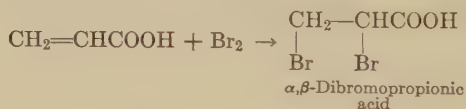


What appears to be an exception to Markownikoff's rule may be explained as an addition to a conjugated system:

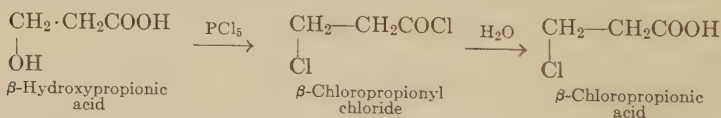


The O at number 4 is more negative than the C at number 1, and invariably adds on the more positive part of the compound.

α,β -Halogenated acids may be prepared thus:



Halogenated acids may also be prepared from hydroxy acids:

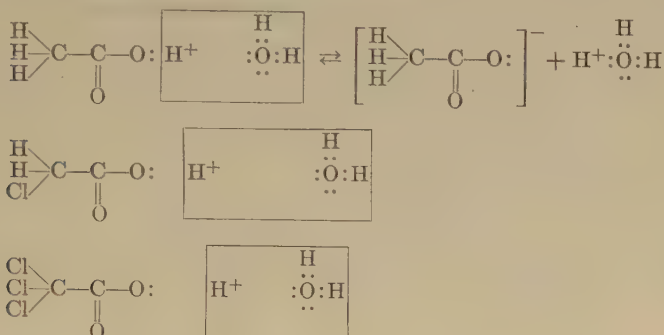


Properties. Some of the properties (such as the formation of salts, esters, etc.) are due to the presence of a carboxyl group and some to the radical attached to the carboxyl group. For example, the greater the number of halogens replacing the hydrogens in the methyl group, the stronger the acidity. Trichloroacetic acid, CCl_3COOH , is a strong acid.

Its strength may be explained as follows: There are all gradations between the strictly electrovalent type of compound and the covalent type of compound. For example, when acetic acid is dissolved in a relatively small quantity of water, but little ionization takes place, and the H of the carboxyl group remains largely as part of the acetic acid molecule. If, however, we replace one H in the methyl portion of acetic acid by a chlorine atom, the H^+ of the COOH is no longer held so firmly by the rest of the molecule since the Cl is strongly electronegative and

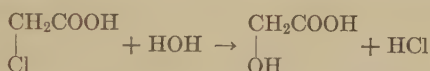
will tend to draw electrons toward itself, which in effect means a loosening of the H^+ . This is still more marked when we form trichloroacetic acid (which has three electronegative Cl atoms) in which the H^+ of the COOH group has completely separated from the molecule and has linked itself with the solvent, producing a highly ionized substance.

The three stages can be represented as:

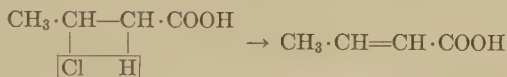


As shown above, the relative distances from H^+ to $-\text{C}-\text{O}: \text{denote}$ the relative firmness of the union. In general, the dissociation of carboxylic acids is increased by substituents.

The α -halogen acids yield the corresponding hydroxy acids by treatment with hot alkali:



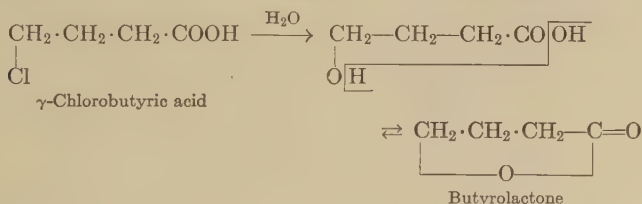
The β -halogen acids yield unsaturated acids when heated with water or alcoholic KOH:



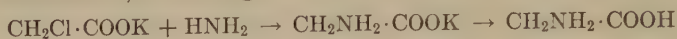
Butenoic acid (Crotonic acid)

In certain cases—where, for example, sodium carbonate is used— CO_2 is also evolved, so that butenoic acid is converted to an unsaturated hydrocarbon, $\text{CH}_3 \cdot \text{CH} = \text{CH}_2$.

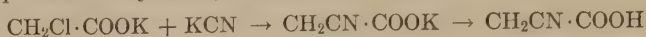
The γ -halogen acids form inner esters or lactones with water:



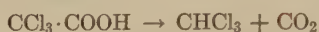
With ammonia, the halogen-substituted acids form amino acids:



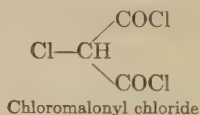
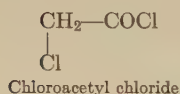
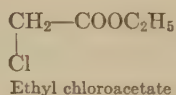
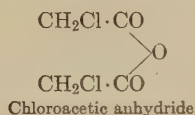
With potassium cyanide, we get cyano acids:



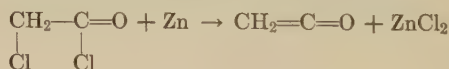
Very many of these halogen-substituted acids are known. Monochloroacetic acid, $\text{CH}_2\text{Cl}\cdot\text{COOH}$, is used in the manufacture of synthetic indigo. The vapors attack the eyes, and they also act corrosively on the skin. Trichloroacetic acid, $\text{CCl}_3\cdot\text{COOH}$, also acts corrosively on the skin; it is used to remove warts and other growths. It has come into use as a protein precipitant. When trichloroacetic acid is boiled with water, chloroform results:



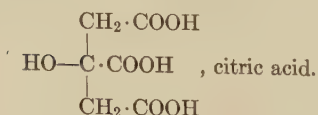
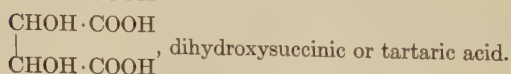
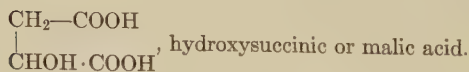
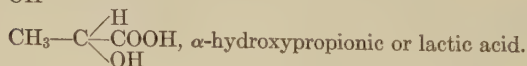
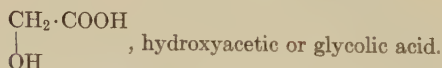
Many other halogenated acids of higher molecular weight are known. It is also possible to have halogenated acid derivatives. For example,



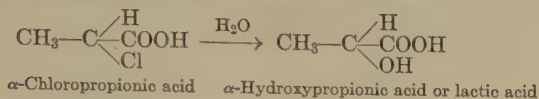
An interesting reaction is that of chloroacetyl chloride with zinc, which offers a convenient preparation of ketene:



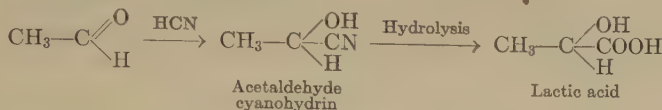
HYDROXY ACIDS



General Methods of Preparation. Several methods suggest themselves readily. 1. Hydrolysis of halogen acids (base):

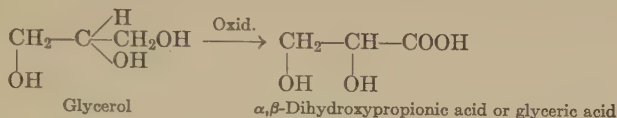


2. Hydrolysis of cyanohydrins:

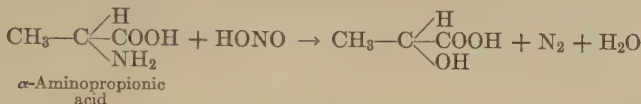


By this method, which obviously yields only α -hydroxy acids, we obtain compounds of one C more than the original carbonyl compound.

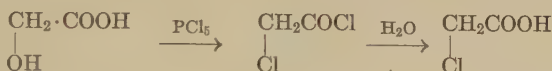
3. Oxidation of a primary alcohol containing another hydroxyl group; e.g.,



4. Action of nitrous acid on amino acids (p. 168):



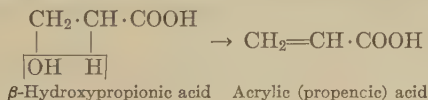
Properties. As might be expected, hydroxy acids show the properties both of hydroxy and of carboxylic substances. Chloro acids are formed with PCl_5 :



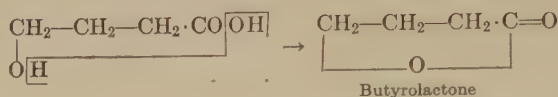
When α -hydroxy acids are heated, two molecules condense with the elimination of two molecules of water to form lactides:



When β -hydroxy acids are heated, we get unsaturated acids:



When γ -hydroxy acids are heated, an inner anhydride (lactone) is formed:



The reverse action (H_2O) can be used to prepare γ -hydroxy acids, since the lactones can be made from γ -halogen acids. δ -Hydroxy acids also form lactones.

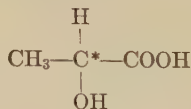
Hydroxyacetic acid, $\text{CH}_2\text{OH}\cdot\text{COOH}$ (also known as **glycolic acid**), occurs in unripe grapes.

α -Hydroxypropionic acid, $\text{CH}_3-\text{C}\begin{array}{l} \text{H} \\ \diagup \\ \text{COOH} \\ \diagdown \\ \text{OH} \end{array}$ (better known as **lactic acid**), is known in three forms, the dextro and the levo optically active modifications, and the racemic, or inactive form (which can, however,

be resolved into the two optically active forms).

Optical Isomerism. The three varieties of lactic acid have similar chemical and physical properties but behave quite differently towards polarized light.¹ One turns the plane of polarized light to the right (and is, therefore, known as dextro or *d*-lactic acid); the other turns it to the left (levo or *l*-variety); and the third, made up of equal parts of the dextro and levo forms, is inactive (*dl*).

Le Bel and *van't Hoff*, quite independently of each other, suggested that all optically active substances have at least one carbon in the molecule attached to four different atoms or groups.² For example, in lactic acid

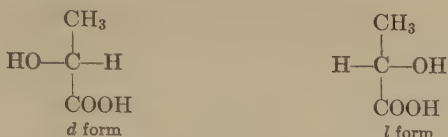


we have a carbon atom marked * which is attached to H, OH, CH_3 , and COOH. Such a carbon atom is known as an **asymmetric carbon atom**.

¹ By polarized light we mean light in which all the vibrations lie in one plane. An ordinary ray of light vibrates in every direction. Polarized light may be obtained by passing ordinary light through a Nicol prism or tourmaline plate, as in the instrument known as the "polarimeter." An optically active substance has the power of rotating this plane of polarized light, the extent depending, among other things, upon the nature of the substance. For further details, consult a practical physical chemistry textbook, for example, Daniels, Mathews, and Williams, *Experimental Physical Chemistry*.

² This idea is connected directly with the *Le Bel-van't Hoff* theory of the tetrahedral carbon atom.

Structurally, the *d* form of lactic acid is related to the *l* form as an object is to its mirror image:



The absolute configurations of most optical isomers are not known; they are not really necessary, since, after all, the important point is to emphasize the *relative* structures of *d* and *l* isomers. These are known as *enantiomorphs* or *optical antipodes*. Optical and geometrical (p. 108) isomerisms are both explained on the basis of the tetrahedral carbon atoms, that is, three-dimensional models, and are therefore known as the two different categories of stereo- or spatial isomerism.

Usually, when a compound containing an asymmetric carbon atom is synthesized, equal parts of the dextro and levo varieties are obtained. Such a mixture is designated as *dl*, or *i* (inactive), and is known as "racemic." This inactive mixture can, as a rule, be resolved into the active constituents in a number of different ways. One of these depends upon the property which certain organisms possess of consuming one component more rapidly than another. For example, some bacteria destroy the *l*-lactic acid, and *Penicillium* (a mold) the *d*-lactic acid.

A much more effective and general method of resolution depends upon the fact that the introduction of the same new asymmetric system into two enantiomorphs destroys the object-mirror image relationship and the identity of the physical properties. For instance, treatment of a racemic mixture (+A - A) with an optically active base (+B) yields a mixture of two salts (+A + B and -A + B) which are optically active isomers but are not enantiomorphs; their physical properties usually differ sufficiently to permit a separation by fractional crystallization; differences in solubility will cause one compound to crystallize from solution before the other.

Such optical isomers which do not stand to each other in the object-mirror image relationship are called *diastereoisomers*.

Racemic acids are generally resolved by the formation of diastereoisomeric salts with such optically active bases as brucine, cinchonine, strychnine, and other alkaloids, or by the formation of diastereoisomeric esters with *d*- or *l*-alcohols.

Racemic bases form salts with such optically active acids as *d*-tartaric or *d*-bromocamphorsulfonic acids (camphor, p. 361). Other types of compounds are treated with such optically active reagents as yield fairly

insoluble derivatives; for example, amines react with aldehydes, and vice versa.

The souring of milk is due to the formation of lactic acid (the inactive variety), and this is brought about by the action of certain bacteria (which are also present in the air) on the milk sugar or lactose in the milk. The acid so formed precipitates the principal protein (casein) in milk, giving rise to what is known as "curdling." The synthetic lactic acid of commerce is prepared from acetaldehyde by hydrolysis of its cyanohydrin.

Lactic acid is manufactured in the United States by the comparatively high-temperature fermentation of cane or beet sugar, corn starch, or corn sugar, with a pure culture of lactic acid bacteria. It is a colorless, viscous liquid, and is used in medicine, dyeing, and calico printing. The antimony, zinc, and iron lactates are used as mordants. Silver lactate is a powerful antiseptic. Ethyl lactate is one of the best solvents for nitrocellulose and is therefore extensively used in the lacquer industry.

d-Lactic acid (also called sarcolactic acid and paralactic acid) is found in muscle tissue, meat extract, blood, and urine. Inactive muscle is alkaline, and after activity muscle becomes acid, a change which has been ascribed to the formation of lactic acid. When the *d* acid is heated it loses its optical activity and is converted to the inactive or *dl* variety.

l-Lactic acid is obtained when sugar is fermented with *Bacillus acidilvolactici*.

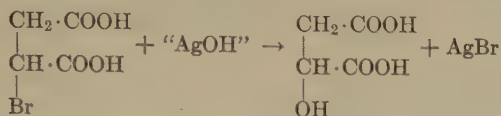
The *d*- and *l*-lactic acids and the *dl* or *i* variety show the same physical and chemical properties; they differ only as regards optical activity.

The intermediate changes that proteins, fats, and particularly sugars undergo in the body in their ultimate breakdown to carbon dioxide, water, and simple nitrogenous bodies are associated with the formation of lactic acid, among other substances. Evidence is accumulating to show that lactic acid is an important intermediate product in the decomposition of the common foodstuffs within the body.

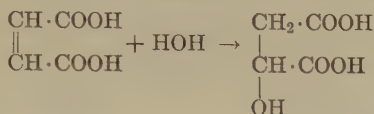
An isomer of lactic acid is β -hydroxypropionic acid, or hydracrylic acid, $\text{CH}_2\text{—CH}_2\cdot\text{COOH}$, in which the hydroxyl group is in the β -position.

Hydroxysuccinic acid, $\begin{array}{c} \text{CH}_2\cdot\text{COOH} \\ | \\ \text{CH}(\text{OH})\cdot\text{COOH} \end{array}$ (commonly known as **malic acid**), is present in unripe apples, cherries, grapes, etc. It may be pre-

pared from bromosuccinic acid by the action of wet silver oxide:

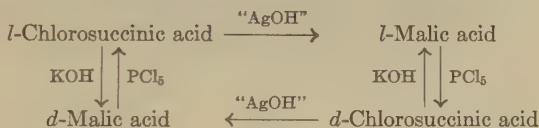


The commercial method of preparation is from maleic acid:



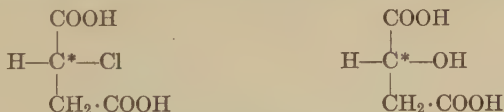
Malic acid is optically active and has the general properties of hydroxy acids. It is used as a flavoring material for foodstuffs.

Walden's Inversion. In studying the reaction of bases on chlorosuccinic acid, *Walden* found that *l*-chlorosuccinic acid, $\begin{array}{c} \text{CH}_2\cdot\text{COOH} \\ | \\ \text{CHCl}\cdot\text{COOH} \end{array}$, when treated with "AgOH" gives *l*-malic acid, $\begin{array}{c} \text{CH}_2\cdot\text{COOH} \\ | \\ \text{CHOH}\cdot\text{COOH} \end{array}$. However, if KOH is substituted for AgOH, *d*-malic acid is obtained. *d*-Chlorosuccinic acid yields *d*-malic acid with AgOH and the *l* variety with KOH. *Walden* also showed that PCl₅ converts *l*-malic acid into *d*-chlorosuccinic acid, and vice versa. To summarize:



This is known as *Walden's inversion*.

It will be noticed that the atoms involved (Cl, OH) are attached to the asymmetric carbon atom:



Similar results have since been obtained with other compounds.

Incidentally, we have in the *Walden* inversion evidence that displacement (substitution) reactions do sometimes effect a change in the relative atomic arrangement of the molecules involved.

The difference should be emphasized between a *Walden* inversion, in which the successive chemical transformations bring about a reversal



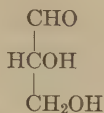
LOUIS PASTEUR (1822-1895)

Chemist, founder of the modern science of bacteriology, and one of the greatest scientists of all times. One of his earliest researches dealt with the crystalline forms of tartaric acid and its salts (p. 152), and this led directly to Le Bel and van't Hoff's conception of stereoisomerism.

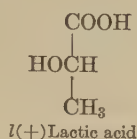
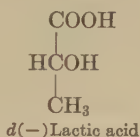
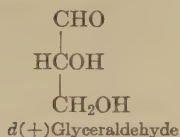
of the sign of optical rotation, and an ordinary racemization, in which a *d* or *l* compound, on standing in solution, forms an equilibrium mixture of *d* and *l* isomers.

In this connection, it is of interest to point out that displacement of an atom or group not linked directly to an asymmetric carbon sometimes inverts the sign of rotation; for example, dextrorotatory lactic acid forms levorotatory salts; levorotatory amyl alcohol (2-methyl-1-butanol) forms dextrorotatory amyl iodide. This does not involve, as far as is known, any structural change.

This state of affairs makes for much confusion, since configurational relationships are much more important than the values of a physical constant. To remedy this, at least in part, the convention has been adopted of using *d* to designate all structures related to that of *d*-glyceraldehyde.

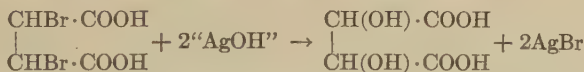


All other optically active compounds in which the corresponding asymmetric carbon has a similar configuration are labeled *d*; their enantiomorphs are, of course, *l*. The sign of rotation is written separately in the name. For instance, *l*-lactic acid is related to *d*(+)-glyceraldehyde and therefore becomes *d*(-)-lactic acid:



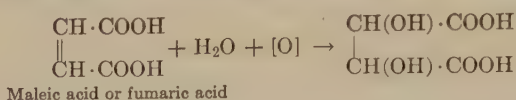
Now the salts of *d*(-)-lactic acid are *d*(+) salts, etc.; and related structures are labeled as such. The value of this system becomes evident when the structures of carbohydrates are considered (Chapter XVII).

Dihydroxysuccinic acid, $\begin{array}{c} \text{CH(OH)} \cdot \text{COOH} \\ | \\ \text{CH(OH)} \cdot \text{COOH} \end{array}$ (commonly known as **tartaric acid**), is a dihydroxy dicarboxylic acid. It can be prepared from dibromosuccinic acid by the action of silver oxide:

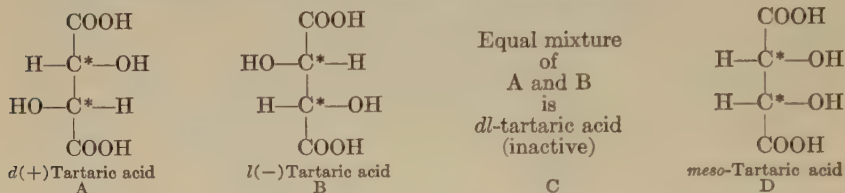


The reduction of tartaric acid (with hydrogen iodide) first yields malic acid and then succinic acid. It is interesting that maleic acid or fumaric

acid, both unsaturated dibasic acids, may be converted to tartaric acid by oxidation with dilute aqueous potassium permanganate:



The following four forms of tartaric acid are known:



Thus we have two forms of tartaric acid which are optically active (A and B); and two which are optically inactive (C and D). A is the mirror image of B, while in D the upper part of the graphic formula is a mirror image of the lower part. C can be resolved into the *d* and *l* forms, but D cannot. C is said to be optically inactive by external compensation; D is optically inactive by internal compensation. In other words, with an even number of asymmetric carbon atoms of similar structure, a molecule can be symmetrical and thus optically inactive; such a compound is known as *meso*.

d-Tartaric acid is found in grapes in the form of potassium acid tartrate. *l*-Tartaric acid may be obtained from the *dl* inactive form by "splitting" or resolution into the active isomers.

Racemic (inactive) or *dl* acid is found in grapes; it is formed when the *d* acid is boiled with NaOH solution. It may be resolved into the *d* and *l* forms.

The fourth variety, *meso*-tartaric acid (first prepared by *Pasteur* by heating the cinchonine salt of *d*-tartaric acid), is also inactive, but, unlike the racemic acid, cannot be resolved into the *d* and *l* forms.

The history of tartaric acid is intimately associated with the development of our ideas of optical activity and of the asymmetric carbon atom; and with these ideas the names of *Pasteur*, *van't Hoff*, and *Le Bel* will forever be linked. It was *Pasteur* who first showed that the racemic acid was really a mixture of two types of crystals, one the image of the other, and that, when mechanically separated¹ and dissolved in water, the one type turned polarized light to the right and the other turned it

¹ *Pasteur* was able to separate two types of sodium ammonium tartrate from crystals he had obtained; such a method of resolution, however, is of little use since it requires large and well-formed crystals.

to the left, suggesting at once that the racemic acid was really a mixture of the *d* and *l* forms. This led *Pasteur* to postulate that such optical activity was related directly to the existence of asymmetric molecules, that is, those in which the object and the mirror image are non-superposable.

The later researches of *van't Hoff* and *Le Bel* connected optical activity with the presence of one or more asymmetric carbon atoms within the molecule; and this is but a restricted case of the more general *Pasteur* rule.

There are two asymmetric carbon atoms in the molecule of tartaric acid; these have already been referred to.

The same principles of asymmetry hold for optically active inorganic molecules too.

Salts of Tartaric Acid. Potassium acid tartrate, $\begin{array}{c} \text{CH(OH)} \cdot \text{COOK} \\ | \\ \text{CH(OH)} \cdot \text{COOH} \end{array}$ (also known as **cream of tartar**), is a constituent of baking powders and is used in dyeing.

Sodium potassium tartrate, $\begin{array}{c} \text{CH(OH)} \cdot \text{COOK} \cdot 4\text{H}_2\text{O} \\ | \\ \text{CH(OH)} \cdot \text{COONa} \end{array}$ (commonly known as **Rochelle salt**), is a constituent of *Fehling's* solution, and is also used as a purgative (in "Seidlitz" powders).

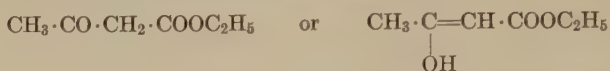
Potassium antimonyl tartrate, $\begin{array}{c} \text{CH(OH)} \cdot \text{COOK} \\ | \\ \text{CH(OH)} \cdot \text{COO(SbO)} \end{array}$ (also known as **tartar emetic**), is used in medicine as an emetic, and also in dyeing.

Citric acid, $\begin{array}{c} \text{CH}_2 \cdot \text{COOH}, \\ | \\ \text{HO} - \text{C} - \text{COOH} \cdot \text{H}_2\text{O}, \\ | \\ \text{CH}_2\text{COOH} \end{array}$ is a monohydroxy tribasic acid, and

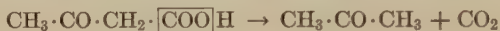
is found in lemons (from the juice of which it is prepared), berries, limes, and other acidulous fruits. It is also prepared on a large scale by the fermentation of glucose or sucrose by certain mold fungi such as *Citromycetes pfefferianus*. It is used in the manufacture of citrates, flavoring extracts, confectionery, soft drinks, and effervescent salts, as a silvering agent, as an ink ingredient in engraving, and in dyeing, calico printing, and medicine.

Magnesium citrate, $(\text{C}_6\text{H}_5\text{O}_7)_2\text{Mg}_3$, is used as a laxative; ferric ammonium citrate, in blueprint paper manufacture and in calico printing. Sodium citrate is used extensively for the prevention of blood coagulation.

Acetoacetic acid, $\text{CH}_3 \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{COOH}$, or acetylacetic acid, and its ethyl ester, acetoacetic ester, $\text{CH}_3 \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{COOC}_2\text{H}_5$, are considered here because the ester may be looked upon as a derivative of a β -hydroxy unsaturated acid (or β -keto saturated acid):

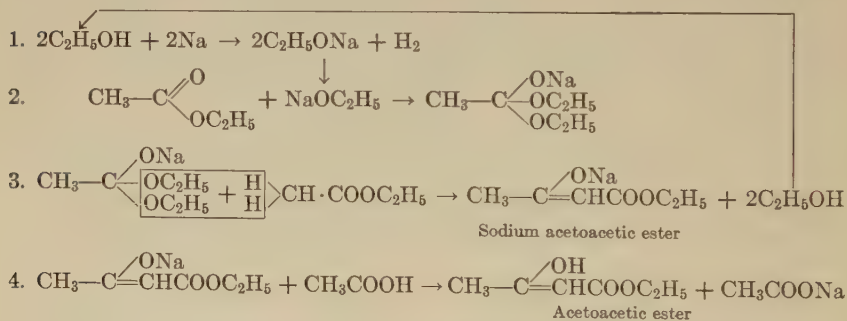


Acetoacetic acid is one of the "acetone bodies" present in the urine of persons suffering from diabetes, and it is commonly known as "diacetic acid." It is an unstable acid and decomposes into acetone:

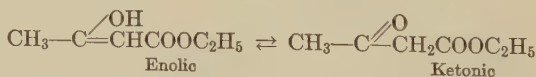


which explains the presence of acetone in the urine and breath of diabetics.

Acetoacetic ester, $\text{CH}_3 \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{COOC}_2\text{H}_5$ (or, more correctly, ethyl acetoacetate), a colorless liquid of fruity odor, is a compound of considerable importance in synthetic organic chemistry. *Claisen's* explanation of its synthesis is the following:



Tautomeric forms:



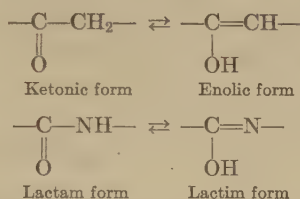
Acetoacetic ester is prepared by the action of sodium on ethyl acetate. A small amount of alcohol is needed for reaction 1; additional quantities of alcohol are formed as shown in 3. This *Claisen* condensation is general for all esters in which there is at least one hydrogen available on the α -carbon, and it may be viewed as another case of aldol condensation, the structural elements involved being a carbonyl group and an alpha C—H. (The NaOC_2H_5 or $\text{C}_2\text{H}_5\text{O}^-$ acts as a base to remove hydrogen; other anhydrous bases react similarly.)

The enolic form of the ester $\left(\begin{array}{c} \text{OH} \\ | \\ -\text{C}=\text{CH}- \end{array} \right)$ first produced (see 4) rearranges to the more stable keto form $\left(\begin{array}{c} \text{O} \\ || \\ -\text{C}-\text{CH}_2- \end{array} \right)$. At room tem-

perature, acetoacetic ester is an equilibrium mixture of enolic and ketonic forms containing 7.5 per cent and 92.5 per cent, respectively.

The type of isomerism wherein, under certain conditions, a compound passes from one structure to another is known as **tautomerism**.

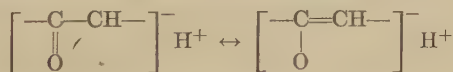
This is characteristic of many compounds having the carbonyl group attached to a carbon or nitrogen atom to which also one or more hydrogens are attached.



An equilibrium between keto and enol forms can be demonstrated experimentally for compounds such as acetoacetic ester and other β -keto acids, β -diketones ($-\text{COCH}_2\text{CO}-$).

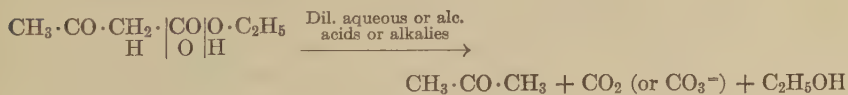
In simple carbonyl compounds there is very little, if any, enol form; for example, acetaldehyde \rightleftharpoons vinyl alcohol. However, many reactions involving carbonyl compounds are explained more satisfactorily on the basis of a similar keto-enol tautomerism which may reasonably be postulated where it cannot be proved.

Such tautomeric forms in equilibrium may also be considered components of a resonating system in the form of the so-called enolate ion:



Uses of Acetoacetic Ester. Depending upon the reagents used, as well as the concentration of solutions, the following two types of decomposition take place:

(a) *Ketonic hydrolysis:*



This is a hydrolysis of the ethyl ester to the unstable acetoacetic acid which decomposes into CO_2 and ketone.

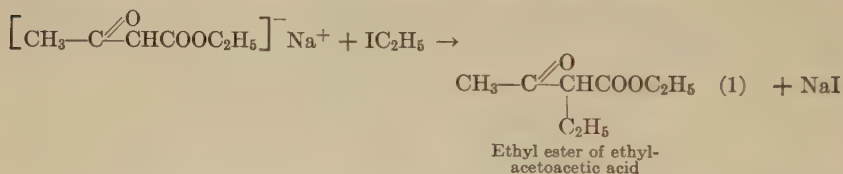
(b) *Acid hydrolysis:*

One or both hydrogens in the $-\text{CO} \cdot \text{CH}_2 \cdot \text{CO}-$ part of the acetoacetic ester may be replaced by various groups, giving rise to substituted acetoacetic ester derivatives. A somewhat analogous case may be found in malonic ester. We recognize once more the hydrogens which are unusually labile because they are linked to a carbon alpha to two negative groups.

If one mole of sodium ethoxide reacts with one mole of acetoacetic ester, the compound

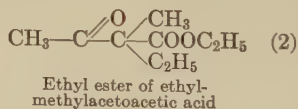


is produced. This reacts with an alkyl halide as follows:

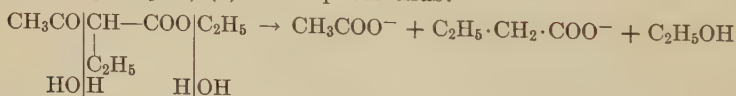


(1) still contains a replaceable hydrogen atom $\left(-\text{C} \begin{array}{c} \text{O} \\ // \\ \text{CH}- \\ | \\ \text{C}_2\text{H}_5 \end{array} \right)$, and

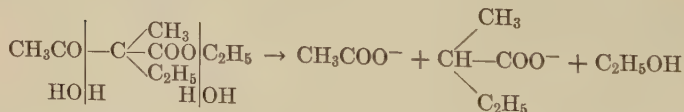
by means of a series of analogous reactions another alkyl group may be introduced, giving, for example:



On *acid hydrolysis*, (1) decomposes thus:

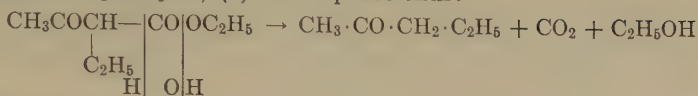


and (2):

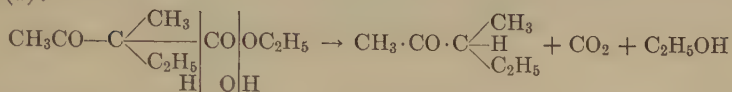


which means that we are able to build up (synthesize) monobasic acids of the types $\text{R}-\text{CH}_2\text{COOH}$ and $\begin{array}{c} \text{R} \\ \diagup \\ \text{CHCOOH} \\ \diagdown \\ \text{R} \end{array}$.

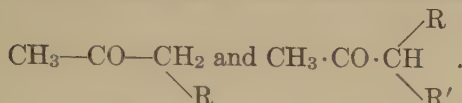
On *ketonic hydrolysis*, (1) decomposes thus:



and (2):



which means that we are able to synthesize higher ketones of the types



Acetoacetic ester is also used in the manufacture of antipyrine and of a number of dyes.

QUESTIONS

- By what reactions would you distinguish the following: (a) $\text{CH}_3 \cdot \text{CHBr} \cdot \text{COOH}$ and $\text{CH}_3\text{CH}_2 \cdot \text{COBr}$; (b) $\text{CH}_2\text{OH} \cdot \text{COOCH}_3$ and $\text{CH}_3\text{OCH}_2 \cdot \text{COOH}$?
- Write structural formulas for the following compounds: (a) acetyl chloride; (b) chloroacetic acid; (c) chloroacetyl chloride; (d) β -chlorobutyric acid; (e) propenoic acid; (f) α -hydroxypropanoic acid; (g) glycolic acid; (h) acetoacetic acid; (i) malic acid; (j) lactic acid; (k) citric acid; (l) tartaric acid; (m) glyceric acid; (n) Rochelle salt; (o) tartar emetic; (p) ethyl chloroformate; (q) butyrolactone; (r) glycolide; (s) dimethylacetoacetic ester; (t) methyl chloroacetate; (u) chloromethyl acetate; (v) γ -chlorohexanoic acid; (w) δ -hydroxypentanoic acid.
- How many monoethyl esters of citric acid could be formulated? How many diethyl esters?
- Discuss and illustrate the stereoisomerism of the tartaric acids.
- Write equations for the following preparations:

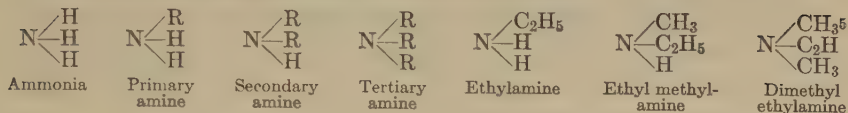
(a) α -chlorobutyric acid	from butyric acid
(b) α -hydroxybutyric acid	" butyric acid
(c) trichloroacetic acid	" acetic acid
(d) monobromoacetic acid	" acetic acid
(e) α, β -dibromopropionic acid	" propenoic acid
(f) β -chloropropionic acid	" propenoic acid
(g) α -hydroxybutyric acid	" propionaldehyde
(h) malic acid	" succinic acid
(i) malic acid	" maleic acid
(j) acrylic acid	" β -hydroxypropionic acid
(k) acetoacetic ester	" ethyl acetate
(l) methyl ethyl ketone	" acetoacetic ester and methanol
(m) butanoic acid	" ethyl acetate
(n) dimethylacetic acid	" acetoacetic ester and methanol
(o) hexanoic acid	" acetoacetic ester and <i>n</i> -butyl alcohol
(p) ethyl alcohol	" propionic acid
(q) butyrolactone	" γ -chlorobutyric acid

6. Write equations for the following reactions: (a) ethyl propionate + sodium ethoxide (Claisen condensation); (b) heating of lactic acid, β -hydroxybutyric acid, γ -hydroxybutyric acid; (c) γ -valerolactone + aqueous sodium hydroxide.
7. Write the structures of all the possible stereoisomers of (a) 2,3-dihydroxybutyric acid; (b) 2,3,4-trihydroxypentandioic acid.
8. State the number and type of possible stereoisomers for each of the following compounds: 2-pentene; 2-methyl-1-butanol; diethyl tartrate.

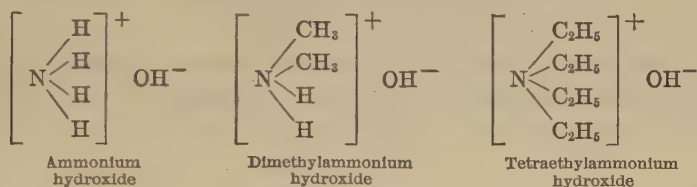
CHAPTER XIII

AMINES

These compounds are derivatives of ammonia:

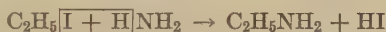


In $\text{R} \cdot \text{NH}_2$ the $-\text{NH}_2$ is an amino group; in $\text{R} \begin{array}{c} \diagup \text{R} \\ \diagdown \text{NH} \end{array}$ the $=\text{NH}$ is an imino group. We have similar relationships in NH_4OH , where one or more hydrogens in the NH_4 group may be replaced by R groups.

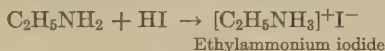


These compounds are known as quaternary ammonium compounds.

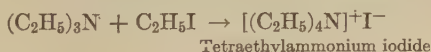
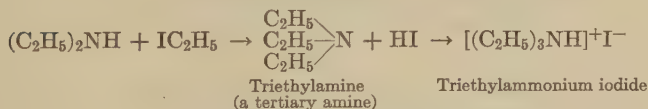
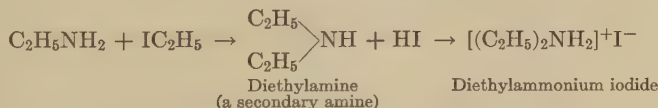
Preparation of Amines. 1. Theoretically the simplest method should be the ammonolysis of alkyl halides:



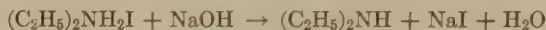
Owing to the basicity of the amine, an ammonium salt is formed:



The reaction, however, proceeds further to yield secondary and tertiary amines, and even quaternary compounds.

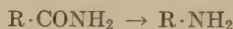


Since all these reactions go on more or less simultaneously, it becomes difficult to isolate the different amines. They can be obtained from the ammonium compounds by treatment with alkali, just as ammonia is obtained from ammonium salts; e.g.:

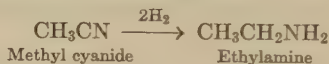


In liquid ammonia, the higher alkyl halides give satisfactory yields of primary amines. Primary amines can also be made by using hexamethylene tetramine (p. 90) instead of ammonia.

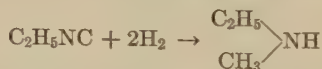
2. The action of halogen and a strong base on an amide yields primary amines containing one C less:



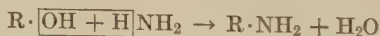
3. The reduction of alkyl cyanides, by catalytic hydrogenation or treatment with sodium and alcohol, yields primary amines:



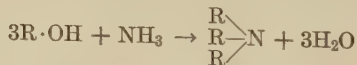
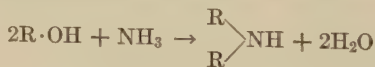
Oximes, nitro compounds, and other compounds containing a C—N linkage can also be reduced. A similar reduction of isocyanides yields secondary amines (in which one alkyl group is methyl).



4. Aliphatic amines are also prepared by the catalytic dehydration of an alcohol and ammonia:



By controlling concentrations and changing the conditions, varying amounts of secondary and tertiary amines may also be obtained.



5. The *Gabriel* synthesis (p. 299) offers a convenient preparation of primary amines. (For another method of preparing secondary amines, see p. 268.)

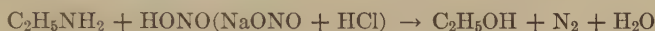
Properties of Amines. These compounds are more basic than ammonia and are readily soluble in water.



They have a strong, fishlike odor, and their vapors are flammable. They combine with acids, giving such salts as methylamine hydrobromide, methylammonium bromide, or $\text{CH}_3\text{NH}_2 \cdot \text{HBr}$, $\text{CH}_3\text{NH}_3\text{Br}$; methylammonium nitrate, $\text{CH}_3\text{NH}_3\text{NO}_3$; and methylammonium sulfate, $(\text{CH}_3\text{NH}_3)_2\text{SO}_4$.

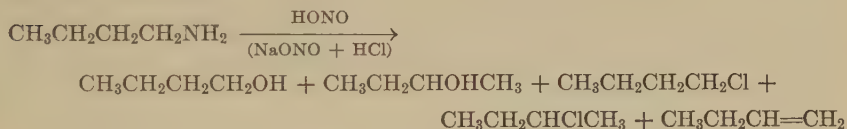
In fact many of the practical applications of the amines are due to their ability to neutralize acids. They are used as corrosion inhibitors, in gas purification to remove H_2S or CO_2 , in the formation of emulsifiers for polishes, insecticides, and oils. They are also used for the production of dyes, detergents, textile softeners, photographic compounds, rubber products, etc.

Action of Nitrous Acid. With a primary amine, nitrous acid forms the corresponding alcohol:



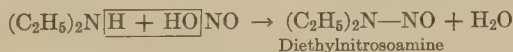
The *Van Slyke* method for determining the rate of hydrolysis of a protein is based on this reaction.

The usefulness of this reaction is greatly restricted by the fact that amines from three carbon atoms up yield not only the alcohol expected by simple displacement but also isomeric alcohols as well as olefins and halides; for example,



Here again is evidence that displacement of one group by another does not necessarily leave the molecular structure unchanged, for molecular rearrangements have obviously taken place (see *Walden inversion*, p. 149).

With secondary amines, nitrous acid forms nitroso compounds:



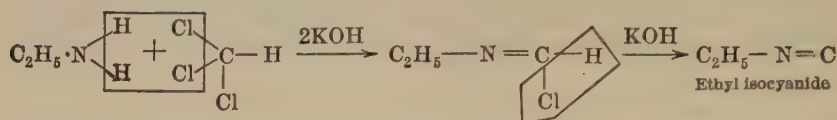
The nitroso compounds are usually yellow, water-insoluble, volatile liquids of aromatic odor.

Tertiary amines simply form salts with nitrous acid:



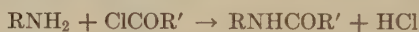
Nitrous acid can therefore be used to distinguish the amines. The *Hinsberg* reaction (p. 258) provides a method of separating, as well as distinguishing, the three classes of amines.

Chloroform and alcoholic potassium hydroxide react with primary amines to form isocyanides (isonitriles).



This is known as the *carbylamine reaction*, and is used to distinguish primary from secondary and tertiary amines. The isocyanides have characteristic and highly disagreeable odors.

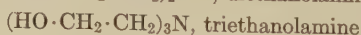
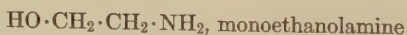
Action of Acyl Chlorides. Amino hydrogens (none in tertiary amines) react readily with the halogen of acyl chlorides of all types to form substituted amides which are useful derivatives of both amines and acids.



Acetyl and benzoyl chlorides are used most generally. In the *Hinsberg* reaction (p. 258), benzenesulfonyl chloride is employed in similar reactions.

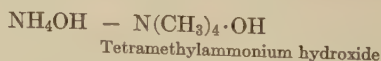
Methylamine is a common constituent of many putrefactive mixtures. Dimethylamine is used in the manufacture of rubber accelerators. Trimethylamine is produced by the destructive distillation of the residue obtained in the sugar-beet industry. The methyl amines are found in herring brine and in the products obtained from the distillation of nitrogenous substances.

By the action of ammonia on ethylene oxide (chart facing p. 80) we get the following:



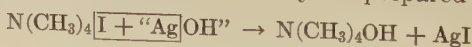
These compounds are viscous, hygroscopic liquids. They are organic bases of mild alkalinity and react with fatty acids to produce soaps which are used in dry cleaning. These soaps are excellent emulsifying agents. Triethanolamine is a very good absorbent for acid gases.

"Quaternary bases" are compounds related to ammonium hydroxide; e.g.,

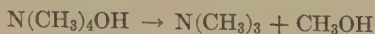


Choline, neurine, and muscarine, compounds of physiological importance (Chapter X), may be regarded as derivatives of quaternary bases.

Tetramethylammonium hydroxide may be prepared thus:



It is a colorless, hygroscopic solid, the solution of which is strongly basic, resembling potassium hydroxide. When heated, it decomposes into trimethylamine:



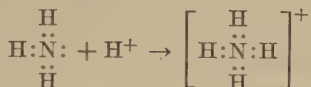
This is really a very good method for the preparation of tertiary amines.

The Electron Configuration of Nitrogen Compounds. When nitrogen combines with hydrogen we get

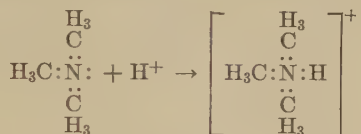


or, each of three hydrogen atoms shares an electron pair with the nitrogen atom, and two electrons remain which are not shared.

In the formation of an ammonium ion (when an acid reacts with NH_3), the essential reaction is the union of the H^+ of the acid with NH_3 :

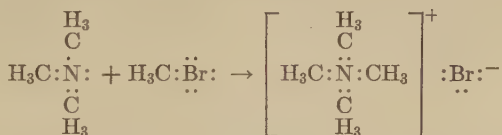


Likewise, in trimethylamine:



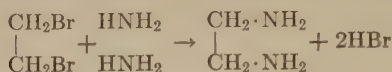
Ammonia and trimethylamine are bases since they both unite with H^+ .

Since trimethylamine (like NH_3) contains two unshared electrons, further combinations may be possible. The combination with methyl bromide to form tetramethylammonium bromide may be represented thus:

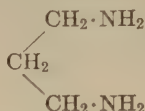


The tetramethylammonium hydroxide, obtained by the action of "AgOH" on tetramethylammonium halides (see above), in water solution, is very largely dissociated and is comparable to NaOH in its concentration of hydroxyl ions. The primary, secondary, and tertiary amines, like ammonia, are less dissociated and, therefore, more weakly basic (p. 15).

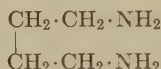
Diamines. Ethylenediamine may be made from ethylene bromide or chloride:



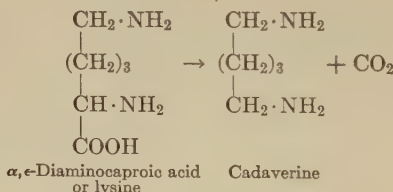
Trimethylenediamine has the formula



Tetramethylenediamine,



or **putrescine**, and pentamethylenediamine, $(\text{CH}_2)_5(\text{NH}_2)_2$, or **cadaverine**, are putrefactive products of the corresponding amino acids, ornithine and lysine (p. 173), and are found among the putrefactive products in the intestine. It is believed that the putrefactive products in the intestine are formed by the action of bacteria on various amino acids, which are converted into the corresponding amines by loss of CO_2 ; e.g.,



In chemical properties the diamines are similar to the monoamines, except that we have to consider two primary NH_2 groups instead of one NH_2 group.

(For a group of compounds related to the amines and of great physiological importance, such as choline, neurine, lecithin, betaine, and muscarine, see Chapter X.)

QUESTIONS

- Write structural formulas for the following compounds: (a) methylamine; (b) isopropylamine; (c) aminoethane; (d) trimethylamine; (e) *n*-propylamine; (f) methyl ethyl amine; (g) cadaverine; (h) ethylenediamine; (i) ethanolamine; (j) diethanolamine; (k) dimethylnitrosoamine; (l) methyl cyanide; (m) *n*-propyl isocyanide; (n) putrescine; (o) triethylammonium chloride; (p) tetramethylammonium hydroxide.
- Two grams of crude methylamine hydrochloride was dissolved in water, made alkaline with sodium hydroxide solution, and distilled, without loss, into 40 ml of *N* HCl solution. Fifteen milliliters of *N* NaOH solution was then re-

quired to make this solution neutral. Assuming that the impurities (such as NaCl) in the crude methylamine hydrochloride were neutral, what was the percentage of methylamine hydrochloride in the crude sample?

3. Describe the preparation of the following compounds:

(a) diethylamine	from ethyl iodide
(b) ethyl isocyanide	" ethylamine
(c) <i>n</i> -propylamine	" butyric acid
(d) <i>n</i> -amylamine	" pentane
(e) <i>n</i> -propylamine	" ethyl cyanide
(f) isopropylamine	" isopropyl chloride
(g) <i>n</i> -propylamine	" 1-nitropropane
(h) ethylamine	" acetaldehyde
(i) methylamine	" methanol
(j) ethanolamine	" ethylene oxide
(k) ethylenediamine	" ethanol
(l) tetraethylammonium hydroxide	" ethyl bromide

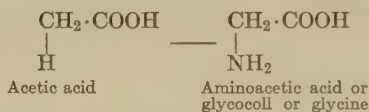
4. Describe by equations a method of distinguishing ethylamine from diethylamine and from triethylamine.

CHAPTER XIV

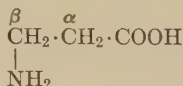
AMINO ACIDS AND PROTEINS

AMINO ACIDS

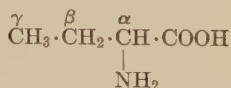
An amino acid is a compound in which a hydrogen in the group attached to the COOH is replaced by an NH₂ group; e.g.,



The nomenclature is analogous to that for the halogen and hydroxy-substituted acids, so that



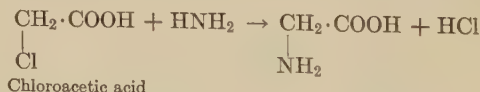
is β -aminopropionic acid; and



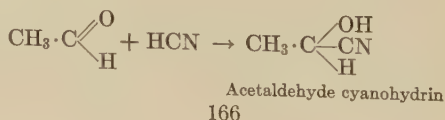
is α -aminobutyric acid.

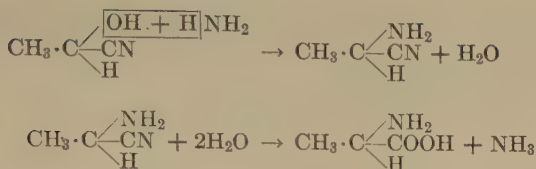
The α -amino acids are of great importance physiologically, since they are the main products obtained when proteins are hydrolyzed.

Methods of Preparation. 1. The action of ammonia on halogen acids is a simple method; e.g.,



2. The action of hydrogen cyanide on aldehydes and ketones, and the subsequent reaction with ammonia and ultimate hydrolysis, offer a convenient synthesis; e.g.,

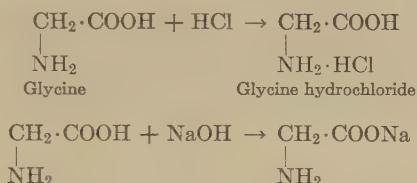




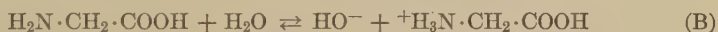
In the *Strecker* synthesis the first two steps are condensed into one by treating the aldehyde or ketone with a mixture of NH_4Cl and NaCN ($= \text{NH}_4\text{CN}$).

3. The hydrolysis of proteins (either by enzymes, acids, or alkalies) yields a succession of substances (metaproteins, proteoses, peptones, polypeptides), the final products being amino acids. In the digestive tract the enzymes pepsin, trypsin, etc., hydrolyze the various proteins of the food into different amino acids.

Properties. Since the amino acids contain NH_2 and COOH groups, they may act as bases or acids; e.g.,

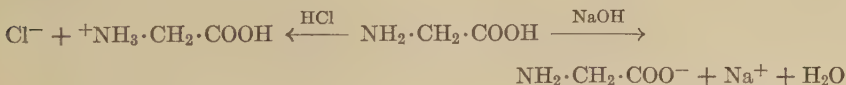


They are, in reality, amphoteric substances like aluminum hydroxide or zinc hydroxide. Glycine, for example, is a feeble electrolyte and is partially dissociated thus:



At some particular hydrogen-ion concentration, the dissociation represented by (A) will be equal to the dissociation represented by (B). This is the "isoelectric point," and at this point the solution is electrically neutral. The concept of the "isoelectric point" in its bearing on the behavior of such substances as proteins is of great importance.

It had been assumed that the addition of HCl to an amino acid causes the ionization of the basic NH_2 group as hydrochloride, and the addition of NaOH causes the ionization of the acid COOH group as sodium salt; thus:



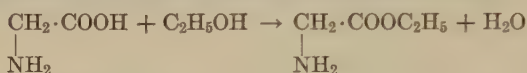
According to the newer theory—the *zwitter ion* or dipolar ion hypothesis—glycine (and other amino acids) in aqueous solution carries both a positive and a negative charge:



and is internally neutralized. Here the addition of acid represses the ionization of the weaker acid. Similarly, when a base is added, it represses the ionization of the weaker base.

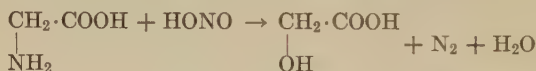


When dissolved in alcohol and saturated with hydrogen chloride (dehydrating agent), the amino acids form esters; e.g.,



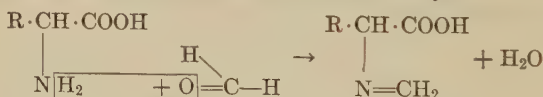
Emil Fischer used this “ester” method to separate the amino acids obtained by the hydrolysis of proteins.

Nitrous acid converts amino acids into the corresponding hydroxy compounds with the liberation of nitrogen; e.g.,



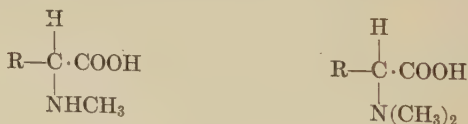
This is the principle of the *Van Slyke* method for the determination of amino acids in blood and tissues, and for following the rate of protein hydrolysis.

Aldehydes react with amino acids to form methylene derivatives; e.g.,

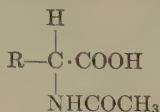


This reaction converts an approximately neutral substance—because of the presence of the NH_2 and COOH groups—into an acid substance by a substitution in the NH_2 group. *Sørensen* used this reaction for determining amino acids in blood, urine, and tissues, and for estimating the extent of protein hydrolysis by titration with alkali. The greater the hydrolysis, the more free NH_2 and COOH groups are formed and hence, when the NH_2 group is removed by formaldehyde, the greater the acidity of the hydrolytic products.

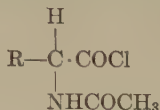
Methylation produces such compounds as



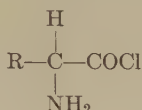
Acetyl chloride or acetic anhydride gives



If this compound is treated with thionyl chloride, SOCl_2 , or phosphorus pentachloride we get



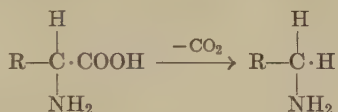
By treatment with aqueous HCl we form



To get the acyl chloride, then, we must first "protect" the amino group.

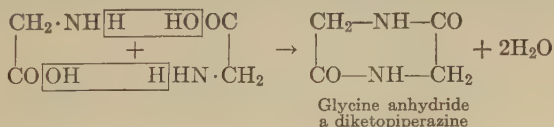
The amino acids form several characteristic crystalline combinations with Reinecke's salt, $[\text{Cr}(\text{CNS})_4(\text{NH}_3)_2]\text{NH}_4$; these reactions are utilized in the isolation of some amino acids.

When heated with barium hydroxide the amino acids are converted to the corresponding amines:

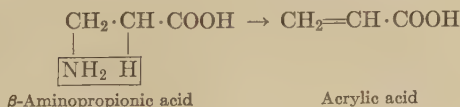


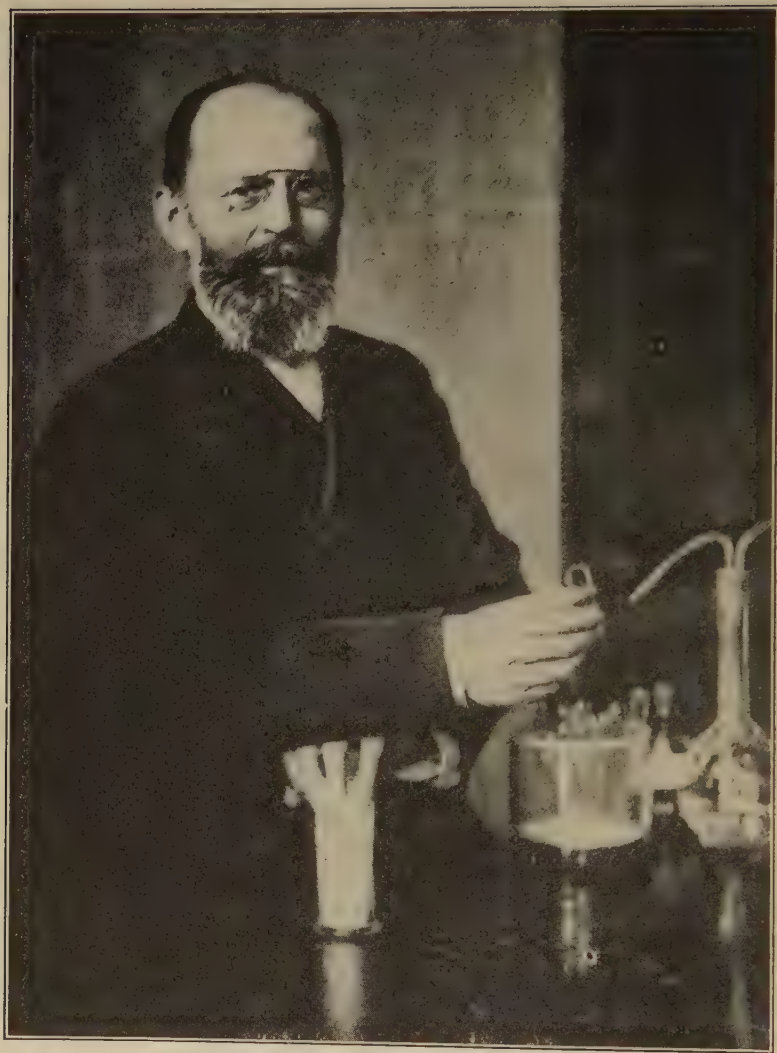
This is a change which is brought about by putrefactive bacteria in the large intestine.

When an α -amino acid is heated, two molecules condense to form an anhydride:



β -Amino acids, when heated, lose ammonia and yield unsaturated acids:

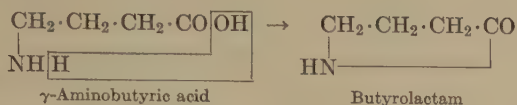




EMIL FISCHER (1852-1919)

One of the foremost organic chemists of the nineteenth century; he did much to elucidate the chemistry of carbohydrates (p. 191), purines (p. 181), and proteins (p. 173).

γ -Amino acids give "lactams":



These reactions are analogous to those of the hydroxy acids (p. 144).

AMINO ACIDS OBTAINED FROM PROTEINS

Glycine, $\begin{array}{c} \text{CH}_2 \cdot \text{COOH} \\ | \\ \text{NH}_2 \end{array}$, also called glycocoll, is aminoacetic acid.

Alanine, $\begin{array}{c} \text{CH}_3 \cdot \text{CH} \cdot \text{COOH} \\ | \\ \text{NH}_2 \end{array}$, α -aminopropionic acid.

Serine, $\begin{array}{c} \text{CH}_2 \cdot \text{CH} \cdot \text{COOH} \\ | \quad | \\ \text{OH} \quad \text{NH}_2 \end{array}$, β -hydroxy- α -aminopropionic acid.

Threonine, $\begin{array}{c} \text{CH}_3 \cdot \text{CH} \cdot \text{CH} \cdot \text{COOH} \\ | \quad | \\ \text{OH} \quad \text{NH}_2 \end{array}$, β -hydroxy- α -aminobutyric acid.

Valine, $\begin{array}{c} \text{CH}_3 \\ \diagup \\ \text{CH} \cdot \text{CH} \cdot \text{COOH} \\ \diagdown \quad | \\ \text{CH}_3 \quad \text{NH}_2 \end{array}$, α -aminoisovaleric acid.

Leucine, $\begin{array}{c} \text{CH}_3 \\ \diagup \\ \text{CH} \cdot \text{CH}_2 \cdot \text{CH} \cdot \text{COOH} \\ \diagdown \quad | \\ \text{CH}_3 \quad \text{NH}_2 \end{array}$, α -aminoisocaproic acid.

Phenylalanine, $\begin{array}{c} \text{CH}_2 \cdot \text{CH} \cdot \text{COOH} \\ | \quad | \\ \text{C}_6\text{H}_5 \quad \text{NH}_2 \end{array}$, β -phenyl- α -aminopropionic acid.

Tyrosine, $\begin{array}{c} \text{CH}_2 \cdot \text{CH} \cdot \text{COOH} \\ | \quad | \\ \text{C}_6\text{H}_4 \cdot \text{OH} \quad \text{NH}_2 \end{array}$, α -amino- β -para-hydroxyphenylpropionic acid.

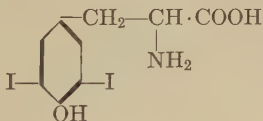
acid.

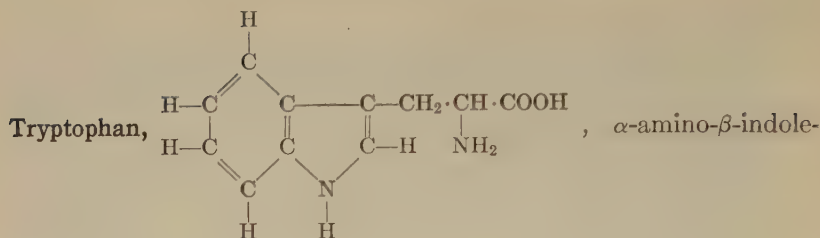
(The student will understand the names of some of these substances after he has studied the sections devoted to aromatic chemistry.)

Thyroxine, $\text{HO} \cdot \text{C}_6\text{H}_2(\text{I})_3 \cdot \text{O} \cdot \text{C}_6\text{H}_2(\text{I})_3 \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{COOH}$, is a hormone (p.

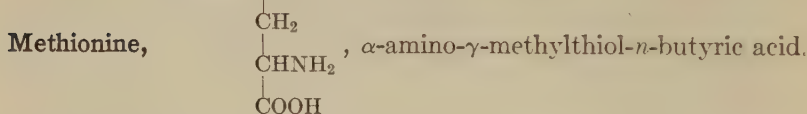
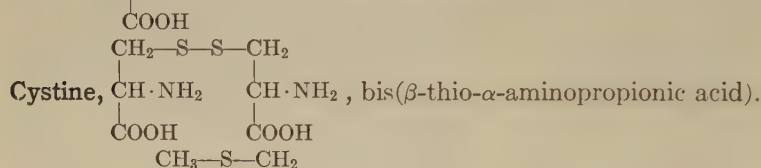
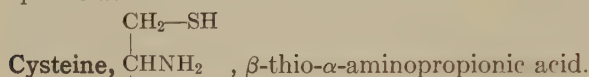
399) chemically related to tyrosine.

Iodogorgoic acid, 3,5-diiodotyrosine, has been obtained from the thyroid gland.

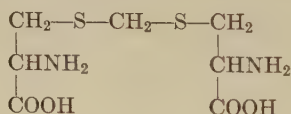




propionic acid.

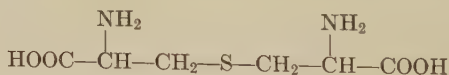


Djenkolic acid, the cysteine thioacetal of formaldehyde,

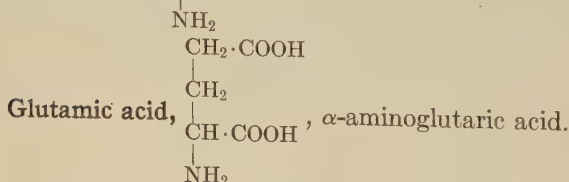
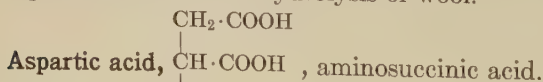


has been obtained from the djenkol bean (*Pithecolobium lobatum*).

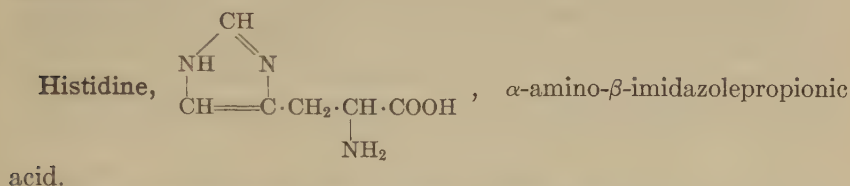
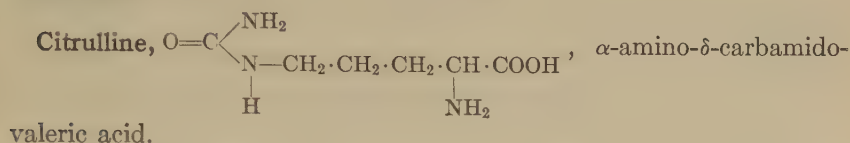
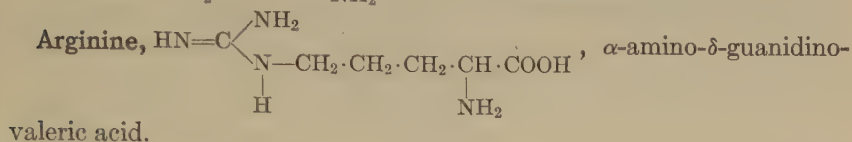
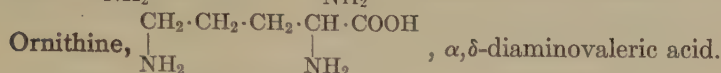
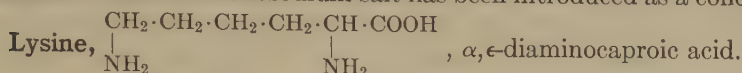
Lanthionine, β -amino- β -carboxyethyl sulfide,



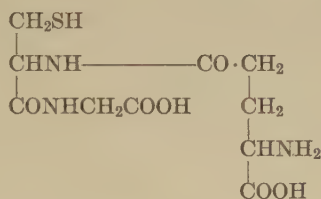
is a product of the acid hydrolysis of wool.



On a commercial scale, glutamic acid is made by the hydrolysis of gluten or soybean. The acid possesses a decided meatlike taste, and because of this the monosodium salt has been introduced as a condiment.



Glutathione, a normal constituent of various plant and animal cells, is a combination (tripeptide) of glycine, cysteine, and glutamic acid, and its formula is



Its chemical name is γ -glutamylcysteylglycine.

PROTEINS

Proteins are essential to life, and, in many ways, they are the most characteristic constituents of protoplasm. They may be regarded as combinations of α -amino acids. Their chemical properties are dependent upon the presence of these amino acids. Their physical properties, on the other hand, are largely due to the fact that they form colloidal solutions. Among the three classes of foodstuffs, *simple* fats, carbohydrates, and proteins, the proteins alone contain the element nitrogen, and, as a

rule, sulfur. The average percentage composition of proteins is C = 53, O = 23, N = 16, H = 7, and S = 1.

Using a special technique (involving the ultracentrifuge), *Svedberg* has shown that the molecular weights of a number of proteins are 34,500 or approximate multiples of this number. Egg albumin is 34,500; hemoglobin, 68,000; serum globulin, 104,000.

The proteins may be classified as follows:

Albumins. Soluble in water and coagulated on boiling. Examples: ovalbumin in egg white, lactalbumin in milk, serum albumin in blood.

Globulins. Insoluble in water, but soluble in dilute solutions of a number of salts (such as sodium chloride) and coagulable on heating. Examples: serum globulin in blood, edestin in hempseed, ovoglobulin in egg white.

Protamines are basic substances forming stable salts with mineral acids. In comparison with some of the other proteins, protamines yield relatively few amino acids on hydrolysis. They are soluble in water and not coagulated on heating. Examples: salmine in salmon sperm; in general, they are found in the heads of ripe spermatozoa and in ova.

Histones. Somewhat similar to protamines. Histones are soluble in water and precipitated by ammonia. Examples: globin in hemoglobin, scombrone in mackerel sperm; thymus histone.

Glutelins are proteins common in the vegetable kingdom. They are insoluble in neutral solvents, but soluble in dilute acids and alkalies. Example: glutenin in wheat.

Prolamines. Prolamines are also common in the vegetable kingdom. They are soluble in 70–80 per cent alcohol (which distinguishes them fromutelins and other proteins) but, like other proteins, insoluble in absolute alcohol. They are also insoluble in water and neutral solvents. Examples: zein in corn, gliadin in wheat and rye, hordein in barley.

Albuminoids are found in the skeletal and connective tissues of animals; they are far more insoluble in reagents than other proteins are. Examples: keratin in hair, collagen in connective tissue.

The proteins which have so far been enumerated are known as "simple proteins," to distinguish them from the following "conjugated proteins":

Nucleoproteins are combinations of protein and nucleic acid, and are characterized by yielding purine bases (p. 181) on hydrolysis. Examples: nucleoprotein in thymus, pancreas, spleen, and glandular tissue in general. They are found in nearly all cells, particularly in the nuclei.

Glycoproteins are combinations of protein and a compound containing the carbohydrate group. They are characterized by yielding, on hydrolysis, a sugar which reduces *Benedict* solution. Examples: mucin in saliva, osseomucoid in bone, tendomucoid in tendon.

Phosphoproteins, like the nucleoproteins, are rich in phosphorus but, unlike them, do not yield purine bases on hydrolysis. Examples: casein in milk, vitellin in egg yolk.

Chromoproteins are combinations of protein with a pigment-containing substance. Example: hemoglobin in blood, which on hydrolysis yields the histone, globin, and the iron-containing substance, heme.

In addition to these, we have a number of ill-defined proteins, obtained in the course of hydrolysis of proteins when acted upon by certain enzymes, acids, or alkalis. They are:

Metaproteins. Metaproteins represent the first stage in protein hydrolysis. They are soluble in acids and alkalis, but insoluble in neutral solvents (from which they are coagulated on boiling).

Proteoses. The primary proteoses are soluble in water, not coagulated on boiling, and precipitated by a one-half saturated solution of ammonium sulfate. The secondary proteoses show similar properties, except that they require a completely saturated solution of ammonium sulfate for precipitation; a crude distinction, it must be confessed.

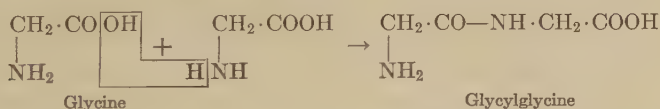
Peptones. Peptones are similar to the proteoses but are not precipitated by ammonium sulfate.

As hydrolysis proceeds, we arrive at the **polypeptide** stage (compounds of a somewhat simpler type, chemically, than peptones), and finally obtain the individual **amino acids**.

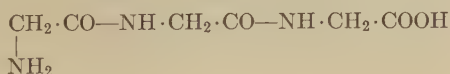
Composition of Proteins. The various proteins, when completely hydrolyzed (by acid, alkali, or enzyme), yield amino acids. One difference among proteins is in the number and in the amount of amino acids which they yield. Up to the present, 23 to 25 of these amino acids have been isolated, and the extent to which they occur in a number of proteins is given in a table (p. 177).

The isolation of the various amino acids is a laborious task.

Constitution of Proteins. *Emil Fischer* showed that the proteins may be regarded as combinations of amino acids, linked in the following way (to take the simplest case):



Glycylglycine (dipeptide) is the simplest example of a polypeptide. It, in turn, may combine with another molecule of glycine to form diglycylglycine (tripeptide):

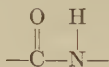


and so on. Of course, the combinations need not involve glycine only, but other amino acids may take a part in such reactions—in fact, any substance containing the NH_2 and COOH groups; so that the number of such possible polypeptides is very large.

Fischer prepared an octadecapeptide, consisting of three leucine and fifteen glycine units. Apart from being a colloid, this octadecapeptide is hydrolyzed by the enzyme trypsin (of the pancreas) into amino acids.

Though proteins have much the same general structure, marked individual variations undoubtedly exist. Casein is a food protein; pepsin, an enzyme in the stomach (p. 390), is also a protein. Other proteins are insulin, the hormone of the pancreas (p. 399), and the tobacco mosaic virus. What makes one protein just a simple food protein, another an enzyme, a third a hormone, a fourth a virus? We do not know. But we must recognize the possibility of differences in the internal structures of the molecules.

General Reactions. *Biuret.* When the protein is mixed with a concentrated solution of sodium hydroxide and a drop or two of dilute copper sulfate solution, a violet or pink color is obtained. Generally, the simpler the protein the more pinkish the color, so that peptones show a distinct pink and albumins a distinct bluish violet. The reaction is given by nearly all substances containing two



groups attached to one another, to the same nitrogen atom, or to the same carbon atom. The name “biuret” is derived from the fact that biuret (which is obtained by heating urea, p. 135), gives this reaction.

Xanthoproteic. Heating a protein solution with concentrated nitric acid produces a yellow color. This is changed to orange on the addition of an excess of ammonium hydroxide. The yellow color is dependent upon the formation of an aromatic nitro compound.

Millon. Heating a protein with *Millon's* reagent (essentially, mercury dissolved in nitric acid) produces a brick-red color or precipitate. This reaction is given by phenol and phenolic derivatives. The substance in the protein molecule responsible for this test is probably tyrosine.

Glyoxylic acid (Hopkins-Cole). When a protein is mixed with glyoxylic acid and concentrated sulfuric acid is added, a violet ring is obtained. This reaction is due to the presence of tryptophan in the protein molecule.

Molisch. With α -naphthol and concentrated sulfuric acid, the protein solution forms a violet ring. The reaction is due to the presence of the carbohydrate glucosamine in the protein molecule.

AMINO ACID CONTENTS OF VARIOUS PROTEINS (PER CENT) *

(From R. J. Williams, *A Textbook of Biochemistry*, Courtesy of D Van Nostrand Company, Inc., New York.)

	Lactalbumin	Egg albumin	Fibrin	Edestin	Gladiin (Wheat)	Zein	Keratin (Horn)	Hemoglobin	Thymus Histone	Saltine	Casein	Vitellin	Gelatin
1. Glycine	0.4	0.0	3.0	3.8	0.0	0.0	0.5		0.5	0.0	0.4	0.0	25.5
2. Alanine	2.4	8.4	3.6	3.6	2.0	9.8	1.6	4.2	3.5	0.0	1.8	0.8	8.7
3. Valine †	3.3	2.5	1.0	6.2	3.3	1.9	4.5			4.3	7.9	1.9	0.0
4. Leucine and isoleucine †	14.0	15.2	15.0	20.9	6.6	25.0	15.3	29.0	11.8	0.0	9.7	9.9	7.1
5. Aspartic acid	9.3	6.2	5.9	10.2	0.8	1.8	2.5	6.4		0.0	4.1	2.2	3.4
6. Glutamic acid	12.9	14.0	14.1	19.2	43.7	31.3	17.2	3.5	3.6	0.0	21.8	13.0	5.8
7. Serine	4.7		0.8	0.3	0.1	2.6	1.1	0.6		7.8	5.8		3.3
8. Threonine †	5.2					4.9					3.9		1.4
9. Proline	3.8	4.2	5.0	4.1	13.2	9.0		2.1	1.5	11.0	8.0	4.2	19.7
10. Hydroxyproline				2.0		0.0		1.0			0.2		14.4
11. Cystine	3.4	2.0	1.5	1.4	2.4	1.0		0.5		0.0	0.3	1.3	0.1
12. Methionine †	2.7	5.2	2.4	2.6	2.0	2.9	7.5					3.0	1.0
13. Phenyl alanine †	1.2	5.2	2.5	3.1	2.3	7.6	1.9	4.2	2.0	0.0	3.9	2.6	1.4
14. Tyrosine	1.9	4.2	3.5	4.5	3.1	3.6	3.6	1.3	5.2	0.0	6.5	3.4	0.01
15. Tryptophan †	2.7	1.3	3.7	1.5	0.8	0.1		2.6			2.2		0.0
16. Arginine	3.2	5.6	7.7	15.8	3.2	1.8	9.8	3.1	15.5	87.4	5.2	7.9	9.1
17. Lysine †	9.2	5.0	10.1	2.2	0.6	0.0	2.7	8.0	6.9	0.0	2.6	5.4	5.9
18. Histidine †	2.1	1.5	2.5	2.1	2.1	1.2	0.6	7.4	1.5	0.0	7.6	1.2	0.9
19. Ammonia	1.3	1.3		2.3	5.2	3.6					1.6	1.3	0.4
Total	83.7	81.8	82.3	105.8	91.4	108.1	68.8	73.9	52.2	110.5	97.1	58.1	108.1

* The data in this table are based partly upon the compilations of Mitchell and Hamilton, *Biochemistry of the Amino Acids*, 1929; Mathews, *Physiological Chemistry*, 1931; Plimmer, *Chemical Constitution of the Proteins*, 1917; and Harrow and Sherwin's *Text-book of Biochemistry*, 1935.

† These amino acids are essential in the diet of experimental rats.

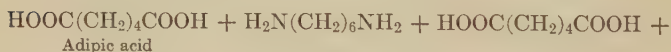
Though no one of these color tests is proof of the presence of a protein, any substance which gives two or more of these tests may be suspected of being a protein. The following reactions are further confirmatory tests.

Proteins are precipitated by the salts of heavy metals, such as lead acetate, mercuric chloride, and copper sulfate. Proteins are precipitated by the "alkaloidal reagents," such as phosphotungstic, phosphomolybdic, tannic, and picric acids. They are precipitated by strong alcohol. A number of the proteins, like the albumins and the globulins, are coagulated on heating.

Proteins from beef blood have been introduced as food products. Serum albumin is mixed with dried egg yolks and used in preparing cakes, cookies, omelets, etc.

An even more important industrial development in the use of proteins is the production of plastics from the casein of skim milk and the protein from soybean by hardening them with formaldehyde. The material is really a synthetic horn with advantages over horn itself. "Karolith" softens when moderate heat is applied and can therefore be bent and embossed. It can be dyed or stained and is now used quite extensively in the manufacture of a variety of buttons, pens, pencils, cigarette holders, etc.

Nylon, a synthetic fiber, is made by reacting diamines with dicarboxylic acids; it is a polyamide of proteinlike structure. It has great strength and elasticity, and the filaments can be drawn as fine as a spider's web. In the manufacture of Nylon, adipic acid is made to combine with hexamethylenediamine:



The reaction involves the carboxyl groups of adipic acid and the amino groups of hexamethylenediamine. The molten product is finally formed into fine filaments.

QUESTIONS

- Write structural formulas for the following compounds: (a) alanine; (b) cystine; (c) butyrolactam; (d) glycine hydrochloride; (e) aspartic acid; (f) glutamic acid.

2. Write equations for the preparation of the following compounds:

- | | |
|----------------------------------|--------------------------------|
| (a) α -aminobutyric acid | from propionaldehyde |
| (b) β -aminopropionic acid | " acrolein |
| (c) butyrolactam | " γ -chlorobutyric acid |
| (d) glycylglycine | " acetic acid |
| (e) diglycylglycine | " glycine |
| (f) lactic acid | " alanine |
| (g) isobutylamine | " valine |

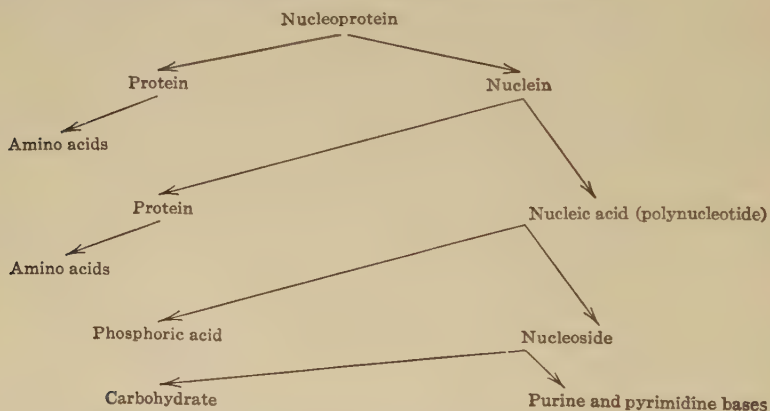
3. Write possible structural formulas for a tripeptide which on hydrolysis yields one molecule each of glycine, alanine, and cysteine.

CHAPTER XV

NUCLEOPROTEINS, PURINES, URIC ACID, AND PYRIMIDINES

Nucleoproteins constitute a group of combined proteins of especial interest to us, since, on the one hand, they are the principal constituents of the nuclei of cells (animal and plant), and, on the other, they yield, on decomposition, a group of important organic substances (purines and pyrimidines). They may be extracted from animal or vegetable sources by water or dilute alkali, and precipitated by acid. For example, the nucleoprotein in yeast may be extracted with dilute alkali and then precipitated by acid; or the lymphatic glands of the ox or sheep, or the thymus of a calf, may be extracted with water, and the nucleoprotein precipitated with acid.¹

A careful study of the hydrolytic products of nucleoproteins shows that they, like the proteins and higher carbohydrates, "split up" in stages. The following is a schematic representation:



The nucleoprotein, in other words, may be regarded as a combination of protein and nucleic acid, the latter, in turn, being a combination of phosphoric acid, carbohydrate, purine, and pyrimidine bases.

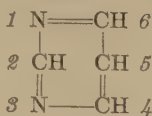
Nucleic acid can be hydrolyzed into four *nucleotides*, each nucleotide consisting of a combination of phosphoric acid, a sugar, and a purine (or pyrimidine) derivative. *Nucleosides* can also be obtained. The

¹ Stanley has shown that the tobacco-mosaic disease virus is a nucleoprotein.

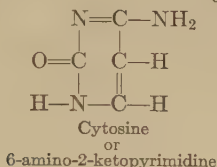
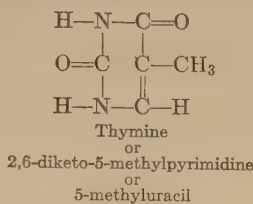
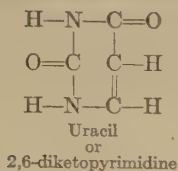
nucleoside is a combination of a carbohydrate and a purine (or pyrimidine) derivative.

Some nucleotides, like adenylic acid, are important constituents of muscle.

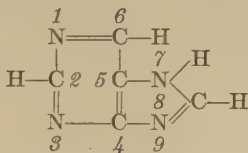
Among the common **pyrimidines** are uracil, thymine, and cytosine. **Pyrimidine** itself has the formula:



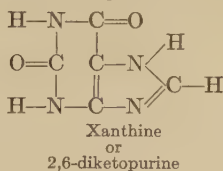
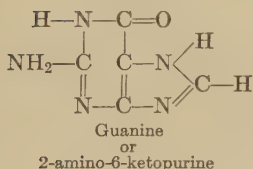
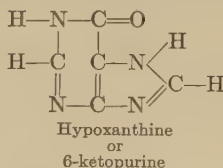
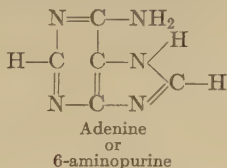
and uracil, thymine, and cytosine have the following structures:



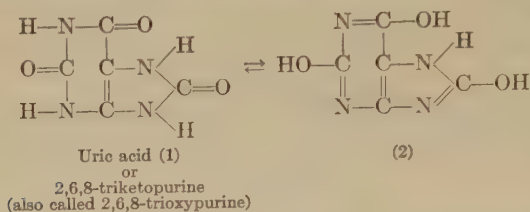
Among the **purine bases** are adenine, hypoxanthine, and guanine. **Purine** itself has the formula:



and the structures for adenine, hypoxanthine, guanine, and xanthine are:



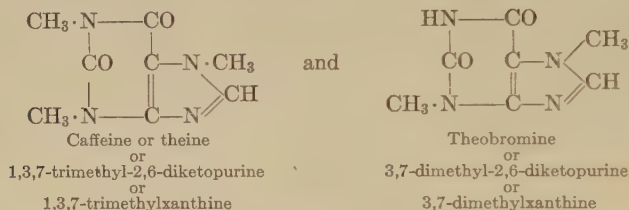
The purines are very largely oxidized to uric acid in the body:



Uric acid is an important nitrogenous constituent of the urine. It may be present in abnormally high amounts in the blood of persons suffering from gout and rheumatism.

Formula 1 for uric acid is the keto or lactam form, and formula 2 is the enol or lactim form. Formula 2 suggests how salts of uric acid can be formed.

Other important purine derivatives are:



Theobromine is present in cocoa beans (chocolate); theophylline (isomeric with theobromine) occurs in tea leaves; caffeine is a constituent of coffee (about 1 per cent) and tea (about 1-4 per cent).

Caffeine, theobromine, and theophylline are strong diuretics, but caffeine is peculiar in having a strong excitant action upon the central nervous system.'

QUESTIONS

1. List the hydrolytic products of nucleoproteins.
2. Write structural formulas for (a) pyrimidine; (b) purine; (c) uric acid (both forms); (d) caffeine.
3. Name some important derivatives of (a) pyrimidine; (b) purine.

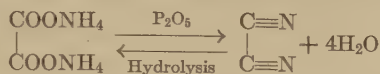
CHAPTER XVI

CYANIDES, ISOCYANIDES, AND OTHER NITROGEN COMPOUNDS

The student who has taken inorganic chemistry is already familiar to some extent with cyanide compounds. He has used potassium ferrocyanide and potassium ferricyanide in testing for iron salts, and he remembers potassium cyanide and hydrogen cyanide as examples of deadly poisons.

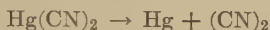
Cyanogen, $(\text{CN})_2$, is a colorless, poisonous gas, with a pungent odor; it burns with a blue flame, giving carbon dioxide and nitrogen. It may be prepared:

1. By heating ammonium oxalate with a dehydrating agent:



The cyanogen can be hydrolyzed back to the ammonium oxalate.

2. By heating mercuric cyanide:

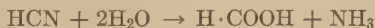


Hydrogen cyanide, formonitrile, HCN (also called **hydrocyanic acid**), is a colorless, poisonous volatile liquid, burning with a violet flame. Its water solution is called prussic acid. (Some attempt was made during World War I to use it as a poison gas.) In combination it occurs in bitter almonds, wild cherry bark, and other plant products. (See glucosides, p. 204.) It is a very weak acid. Its formula may be represented as $\text{H}-\text{C}\equiv\text{N} \rightleftharpoons \text{H}-\text{N}\equiv\text{C}$. It may be prepared by heating sodium cyanide with sulfuric acid:

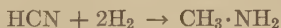


a reaction quite analogous to the preparation of the halogen acids.

Hydrogen cyanide hydrolyzes to formic acid:



and reduces to methylamine:

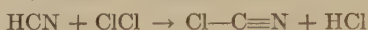


In medicine a 2 per cent solution is used in respiratory diseases and to quiet a cough. It is used as a fungicide and insecticide (spraying

trees). Ships, flour mills, homes, etc., are very often disinfected with HCN gas.

By the action of liquid hydrocyanic acid on calcium carbide (in the presence of a small quantity of water as a catalyst), calcium cyanide, $\text{Ca}(\text{CN})_2$, a solid, is obtained. This substance liberates HCN on mere exposure to the air and, being a solid, can be more easily handled than HCN.

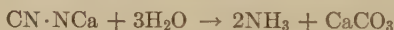
Cyanogen chloride, $\text{CN} \cdot \text{Cl}$, a poisonous liquid of low boiling point, was used as a poison gas in World War I. It may be prepared by the action of chlorine on hydrogen cyanide:



Cyanamide, $\text{CN} \cdot \text{NH}_2$, is prepared by the action of ammonia on cyanogen chloride:



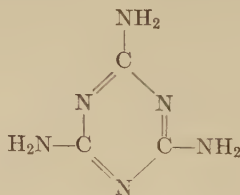
Calcium cyanamide, $\text{CN} \cdot \text{NCa}$, made by heating calcium carbide and nitrogen, $\text{CaC}_2 + \text{N}_2 \rightarrow \text{CaCN}_2 + \text{C}$, finds extensive use as a fertilizer, for in the presence of water it decomposes in the soil, liberating ammonia:



The calcium cyanamide of commerce ($\text{CaCN}_2 + \text{C}$) is sold under the name of "nitrolime."

The dimer of cyanamide, and made from it, is dicyandiamide,

$\text{HN}=\text{C} \begin{array}{l} \nearrow \text{NH}_2 \\ \searrow \text{NHCN} \end{array}$; it is used in the synthesis of barbiturates. The trimer, **melamine**,

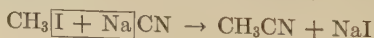


is used in the manufacture of light-colored resins.

ALKYL CYANIDES, $\text{R}-\text{C}\equiv\text{N}$

Nomenclature. CH_3CN may be called either methyl cyanide or cyanomethane or acetonitrile. CH_3CN is acetonitrile because it hydrolyzes to acetic acid. Similarly, $\text{C}_2\text{H}_5 \cdot \text{CN}$ is propionitrile.

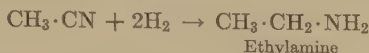
Preparation. 1. As we have already seen (p. 51), alkyl cyanides can be prepared by the action of NaCN on an alkyl halide; e.g.,



2. They are also made by heating the corresponding amide in the presence of a dehydrating agent; e.g.,



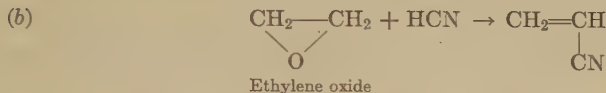
Properties. The reactions of cyanides show unsaturation and are symbolized by the triple linkage:



Acrylonitrile, $\text{CH}_2=\text{CHCN}$, is used in the manufacture of a synthetic rubber (Buna N) in which it forms a copolymer with butadiene. It is prepared by methods such as the following:



Ethylene chlorohydrin



Ethylene oxide

ALKYL ISOCYANIDES, $\text{R—N}=\text{C}\diagdown$, or $\text{R—N}\equiv\text{C}$

Nomenclature. $\text{CH}_3\cdot\text{N}=\text{C}\diagdown$ may be called methyl isocyanide or methyl carbylamine. ($\text{C}_2\text{H}_5\text{—N}=\text{C}\diagdown$ is commonly spoken of as “carbylamine.”)

In organic cyanides the R is connected to the carbon atom:

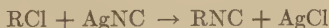


whereas in the organic isocyanides the R is connected to nitrogen,



Formula A is used because the isocyanides are highly reactive substances, forming, among other things, additive compounds on the carbon alone.

Preparation. These compounds are made by: 1. The action of silver cyanide on alkyl halide; e.g.,



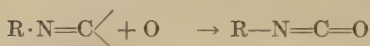
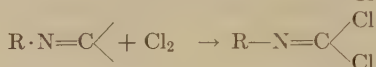
(which suggests that silver cyanide may exist in one of two forms, either as AgCN or AgNC).

2. The reaction of a primary amine with chloroform in an alkaline solution; e.g.,



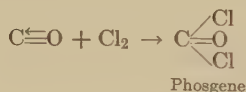
This is a test for primary amines.

Properties. The isocyanides are colorless, poisonous liquids, with an extremely disagreeable and characteristic odor. They are very reactive; e.g.,

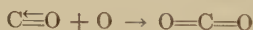


The C in $\text{R} \cdot \text{N}=\text{C} \begin{smallmatrix} \diagup \\ \diagdown \end{smallmatrix}$ seems to be very reactive and, therefore, unsaturated. Compounds of the $\text{R} \cdot \text{N}=\text{C} \begin{smallmatrix} \diagup \\ \diagdown \end{smallmatrix}$ type readily polymerize to $(\text{RNC})_x$ types.

In this connection, it may be of interest to point out here that the reactivity of carbon monoxide may be viewed as the unsaturation of its carbon atom, e.g.,

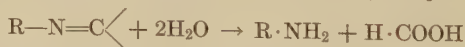


or

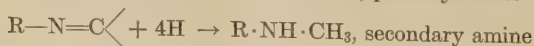


whereby the "divalent" carbon is transformed into the tetravalent form.

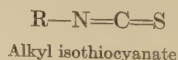
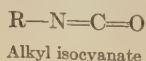
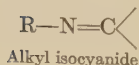
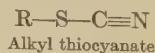
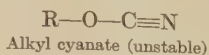
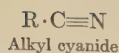
To distinguish between the cyanide and the isocyanide, it is merely necessary to hydrolyze the compounds:



We may also distinguish them by catalytic reduction:

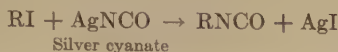


OTHER NITROGEN COMPOUNDS



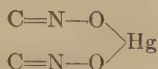
Isocyanic acid, HNCO , is an unstable liquid, but a polymer, cyanuric acid $(\text{HNCO})_3$, is known.

RNCO compounds are prepared thus:

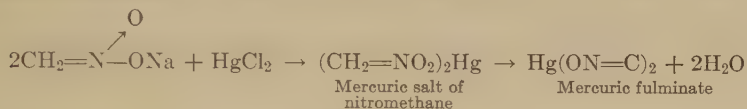


Fulminic acid, $\text{C}=\text{NOH}$, is a poisonous, very unstable liquid. Here again we have a divalent carbon represented.

Mercuric fulminate,



and silver fulminate, $\text{C}=\text{N}-\text{OAg}$, are prepared when the respective metals are acted upon by nitric acid and alcohol. Mercuric fulminate can also be made by the action of the sodium salt of nitromethane with mercuric chloride:

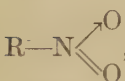
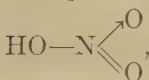


The fulminates are used as detonators in percussion caps to explode gunpowder, dynamite, TNT, and other explosives.

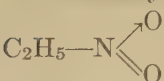
Allyl isothiocyanate, $\text{CH}_2=\text{CH}\cdot\text{CH}_2\cdot\text{N}=\text{C}=\text{S}$, present, in combination, in black mustard seed, is used in medicine as a powerful rubefacient and counterirritant and as a substitute for the mustard plaster.

ALIPHATIC NITRO COMPOUNDS

Aliphatic nitro compounds may be looked upon as nitric acid,

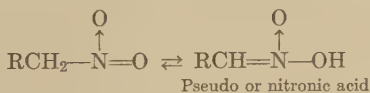


, in which the OH is replaced by R. The nitro compounds, are isomeric with the alkyl nitrites, $\text{R}-\text{O}-\text{N}=\text{O}$, which have already been discussed on p. 115. For example, nitroethane,



, is isomeric with ethyl nitrite, $\text{C}_2\text{H}_5-\text{O}-\text{N}=\text{O}$, though it differs from ethyl nitrate, $\text{C}_2\text{H}_5-\text{O}-\overset{\text{O}}{\text{N}}=$.

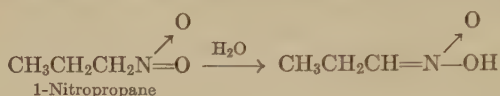
The structure of a primary aliphatic nitroparaffin may be represented as



(Compare with keto-enol tautomerism.) By means of a strong base, such as NaOH, this pseudo acid can be neutralized to form



Alkyl nitronic acids, tautomers of the nitroparaffins, are produced when the nitroparaffins are dissolved in water:

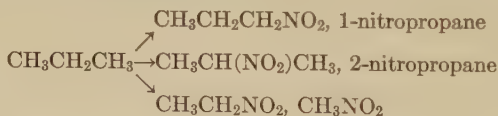


By dehydration, the reaction may be made reversible. However, by neutralizing the nitronic acid with a base, the salt of the nitroparaffin is obtained. The nitroparaffin can be regenerated with weak acids (carbonic acid, for example).

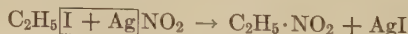
Aliphatic nitro compounds are now made on an industrial scale by the vapor-phase nitration of paraffins with nitric acid, a substitution reaction:



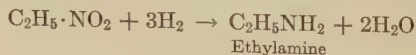
The principal hydrocarbon used is propane, which yields not only the two possible isomeric nitropropanes but also, by some sort of cracking process, nitroethane and nitromethane:



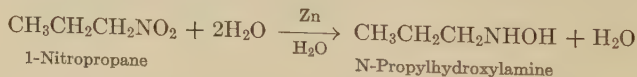
The nitro compounds may also be prepared by the action of silver nitrite on halogen compounds; e.g.,



They are easily reduced to the corresponding primary amines:



If mild reducing agents are used, such as zinc dust and water, we get N¹-alkyl hydroxylamines:



¹ This means that the nitrogen atom is attached to the carbon of the alkyl group

QUESTIONS

1. Write equations to show how ethyl cyanide may be differentiated from ethyl isocyanide.
2. Write structural formulas for the following compounds: (a) sodium cyanide; (b) cyanogen; (c) cyanamide; (d) calcium cyanamide; (e) acetonitrile; (f) methyl isocyanide; (g) carbylamine; (h) methyl cyanate; (i) methyl isocyanate; (j) ethyl thiocyanate; (k) ethyl fulminate; (l) ethyl isothiocyanate; (m) mercuric fulminate; (n) 2-nitropropane; (o) ethyl nitrite; (p) ethyl nitrate; (q) nitrosomethane; (r) dimethylnitrosoamine; (s) ethyl nitronic acid.
3. Describe by equations the preparation of the following compounds:

(a) ethyl cyanide	from ethyl iodide
(b) ethyl cyanide	" propionic acid
(c) ethyl cyanide	" propanal
(d) ethyl isocyanide	" ethyl iodide
(e) methyl isocyanide	" methylamine
(f) ethylamine	" methyl cyanide
(g) phosgene	" carbon monoxide
(h) ethyl isocyanate	" ethyl iodide
(i) cyanogen	" mercuric cyanide
(j) cyanogen chloride	" hydrogen cyanide
(k) calcium cyanamide	" limestone, coke, and air
(l) nitroethane	" ethyl iodide
(m) ethylamine	" nitroethane
(n) acetic acid	" nitroethane

CHAPTER XVII

CARBOHYDRATES¹ AND RELATED COMPOUNDS

The name **carbohydrate** (carbon hydrate) is derived from the fact that compounds belonging to this class contain C, H, and O, the H and O being in the proportion of 2 : 1, respectively (as in water). There are, however, substances other than carbohydrates, such as acetic acid ($\text{CH}_3 \cdot \text{COOH}$) and lactic acid ($\text{CH}_3 \cdot \text{CHOH} \cdot \text{COOH}$), which contain H and O in the proportions found in water. On the other hand, a number of compounds belong to the carbohydrates although the proportion of H to O is not 2 : 1; e.g., rhamnose ($\text{C}_6\text{H}_{12}\text{O}_5$).

The carbohydrates include polyhydroxy aldehydes and polyhydroxy ketones, and compounds which can be converted into such aldehydes and ketones on hydrolysis.

In reality, the simplest carbohydrate is glycolaldehyde, $\text{CH}_2\text{OH} \cdot \text{CHO}$; but this substance is not optically active, for it contains no asymmetric carbon atom. It is therefore customary to regard glyceraldehyde, $\text{CH}_2\text{OH} \cdot \text{CHOH} \cdot \text{CHO}$, as the "mother substance."

Carbohydrates are derived mainly from the vegetable kingdom. Physiologically, the carbohydrates represent one of the three great classes of foodstuffs. Many of them are also of extreme importance in the industries.

In general, carbohydrates fall into two main classes: the sweet and crystalline compounds called sugars; and the tasteless and noncrystalline compounds termed starches, celluloses, and allied products.

Carbohydrates are classified into:

A. *Monosaccharides* (no further hydrolysis with dilute acids):

Trioses, $\text{C}_3\text{H}_6\text{O}_3$, as glyceraldehyde, $\text{CH}_2\text{OH} \cdot \text{CHOH} \cdot \text{CHO}$, or dihydroxyacetone, $\text{CH}_2\text{OH} \cdot \text{CO} \cdot \text{CH}_2\text{OH}$.

Tetroses, $\text{C}_4\text{H}_8\text{O}_4$, as erythrose, etc.

Pentoses, $\text{C}_5\text{H}_{10}\text{O}_5$, as arabinose, xylose, ribose, etc.

Hexoses, $\text{C}_6\text{H}_{12}\text{O}_6$, as glucose, mannose, galactose, fructose, sorbose, etc.

¹ The International Union of Pure and Applied Chemistry proposed the term **glucides** for carbohydrates and glucosides.

B. *Disaccharides*, $C_{12}H_{22}O_{11}$ (yield two molecules of monosaccharides upon hydrolysis):

Sucrose, maltose, lactose.

C. *Trisaccharides*, $C_{18}H_{32}O_{16}$ (yield upon hydrolysis three molecules of monosaccharides):

Raffinose.

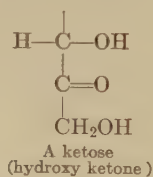
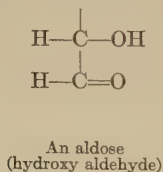
D. *Polysaccharides*, $(C_6H_{10}O_5)_x$ (yield upon hydrolysis more than three molecules of monosaccharides):

Starch, cellulose, dextrin, glycogen, inulin, gums, pectins, pentosans, etc.

The ending *-ose* generally refers to carbohydrates.

MONOSACCHARIDES

The monosaccharides, or simple sugars, are aldehydes or ketones linked directly to carbons with OH groups as:



The trioses and tetroses are of theoretical rather than practical importance.

The **pentoses** in the form of more complex combinations, the *pentosans*, occur extensively in the plant kingdom and are found more particularly in the pectins and gummy substances of plants. The pentoses are obtained from the pentosans by hydrolysis with acids. When they are treated with concentrated hydrochloric acid and distilled, furfural is obtained (p. 332), a process which forms the basis for the estimation of pentoses and pentosans. Among the more common pentose sugars are **arabinose**, obtained by hydrolyzing gum arabic; **xylose**, obtained by the hydrolysis of straw; and **ribose**, a constituent of nucleic acid found in yeast.

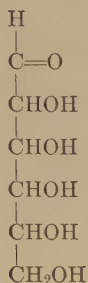
Extremely important, from our point of view, are the hexoses, the disaccharides, and some of the polysaccharides.

Among the **hexoses**, $C_6H_{12}O_6$, **d-glucose**, also called dextrose, is the most important. It is present in the juice of many sweet fruits, such as grapes; hence it is also called grape sugar. It is a normal, and very necessary, constituent of blood, but, in pathological conditions, as in diabetes, it accumulates to an abnormal degree in the blood and in the urine. Glucose is a food which is readily absorbed and is widely used in therapy.

Commercially, glucose is prepared by the hydrolysis of starch in the presence of dilute acids.



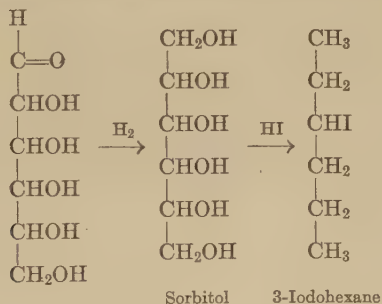
It may be obtained from many poly- and disaccharides. Its formula may be written:



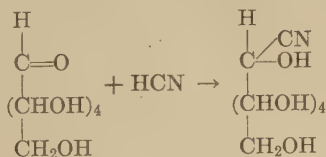
Some indication of how we arrive at such a structural formula may be given. In the first place, elementary analysis and molecular-weight determinations give us the empirical formula $\text{C}_6\text{H}_{12}\text{O}_6$. The substance behaves like an alcohol, because it reacts with acetyl chloride or acetic anhydride to form acetyl derivatives:



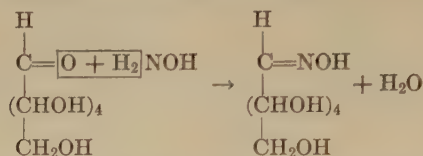
Since glucose forms a penta-acetyl derivative, it must contain five OH groups. On reduction, glucose first yields the corresponding alcohol, and ultimately (if HI is used) a normal six-carbon chain iodohydrocarbon, proving glucose to contain a normal chain of carbon atoms:



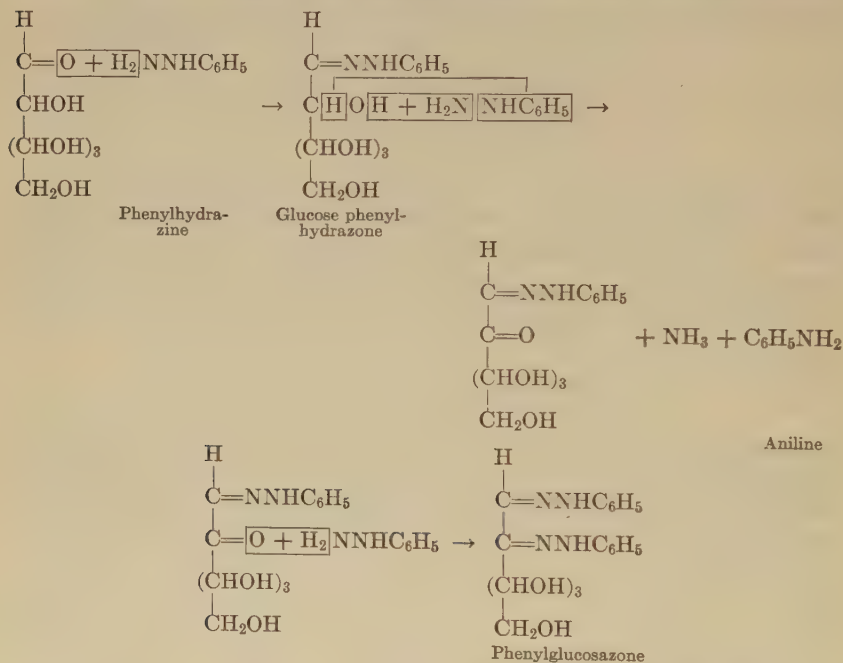
Glucose forms a cyanohydrin with HCN:



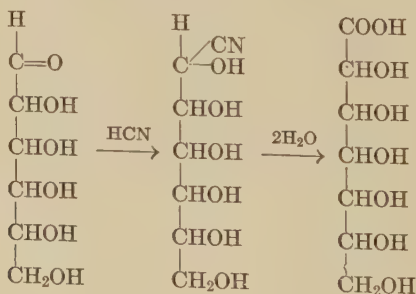
and an oxime with hydroxylamine, NH_2OH :



proving the presence of a carbonyl group. The presence of this group may be further shown by the reaction of glucose with phenylhydrazine:



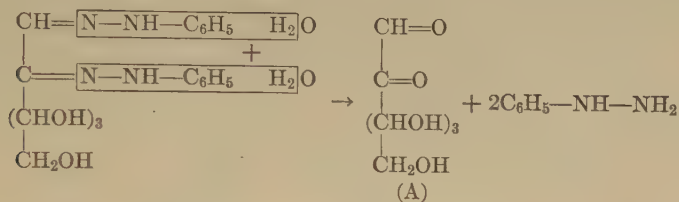
It now merely remains to determine the position of the CO group. This can be done in the following way: glucose is combined with HCN and the resulting product is hydrolyzed.



The hydroxy acid is a normal, seven-carbon compound. The COOH group must be attached to the sixth carbon atom, and this, in turn, must have contained a CO group to have reacted with HCN. But the sixth carbon atom in glucose is the end carbon atom; therefore, the position of the CO group in glucose must be at the end carbon atom.

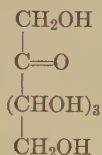
If we have gone into the constitution of glucose at some length, it is merely to illustrate the methods of assigning formulas to the various carbohydrates.

The **osazone**, formed from glucose and phenylhydrazine (p. 273), undergoes a very interesting reaction when warmed with concentrated hydrochloric acid:



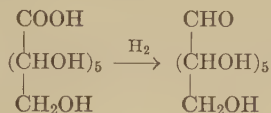
A, known as glucosone, is an example of a class of compounds called **osones**.

By reducing glucosone we change the aldehydic into an alcoholic group and get



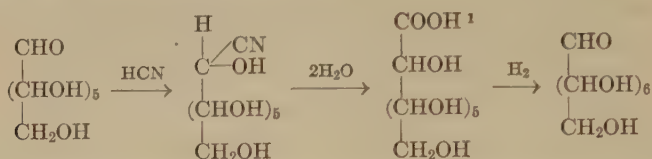
which, as may readily be seen, is a compound isomeric with glucose, but different from it in having a keto instead of an aldehyde group. This compound is none other than fructose (see p. 203). Thus by means of the osone reaction we can pass from glucose to fructose. (Aldose \rightarrow Ketose.)

We have seen how by the use of HCN we can pass from a six- to a seven-carbon compound. Now it is possible to reduce such a compound:



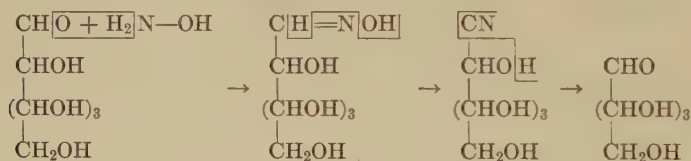
and obtain a product analogous in constitution to glucose except that it contains seven instead of six carbon atoms.

It is evident that this new compound may again be treated with HCN and the various steps repeated:

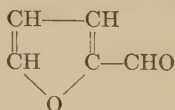


thereby obtaining an eight-carbon compound. Obviously, we have here a method (due to *Kiliani*) by which the carbon content of a sugar may be *increased*—a very important process in synthetic chemistry.

An equally important and interesting procedure is to *decrease* the carbon content of a compound. This may be done by first forming the oxime with hydroxylamine, then converting the product into the nitrile (by loss of water), and finally, by treatment with ammoniacal silver nitrate solution, splitting off HCN:



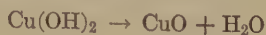
Properties of Glucose. Like all carbohydrates, glucose reacts with the *Molisch* reagent (α -naphthol) and concentrated H_2SO_4 to give a violet ring or color, a reaction said to be due to the formation of furfural



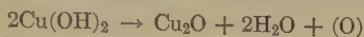
or its derivatives. Glucose forms an osazone with phenylhydrazine, a reaction already discussed. These osazones are of the utmost importance in the identification of a number of sugars, since they show definite crystalline forms and have definite melting points. Owing to the presence of the CHO group, glucose reduces ammoniacal silver solutions and the alkaline solutions of a number of metals, such as copper, bismuth, and mercury. The best known of these reactions is the *Fehling* test, which consists in heating glucose with a solution of copper sulfate to which potassium or sodium hydroxide and Rochelle salt have been added; a yellowish red precipitate of cuprous oxide is obtained. The theory of the reaction may be explained thus: in the absence of a reduc-

¹ Or its lactone.

ing agent, such as glucose, the cupric hydroxide that is first formed would be converted to black cupric oxide:

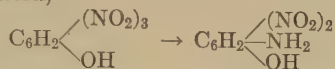


but, when glucose or any other appropriate reducing agent is present, cuprous oxide, Cu_2O , which is yellow to red in color, is formed instead:



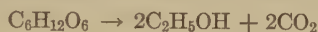
Benedict has modified the *Fehling* reagent by mixing the copper sulfate with sodium citrate and sodium carbonate, producing a reagent which does not deteriorate even after long standing. The *Benedict* modification also has the advantage over *Fehling's* solution in that, when it is used to test for glucose in the urine, neither uric acid nor creatinine—nitrogenous substances present in the urine—interfere with the test; nor does chloroform, which is often used as a preservative for the urine.

Heated with picric acid, in the presence of KOH , glucose gives a red color—a reaction which forms the basis for a colorimetric determination of glucose in blood. The reaction is said to be due to the reduction of picric to picramic acid,



though the question has not been definitely settled.

Yeast “ferments” glucose, forming ethyl alcohol and CO_2 :



Glucose is optically active, turning the plane of polarized light to the right. If its formula is examined, it will be seen that glucose contains four asymmetric carbon atoms:

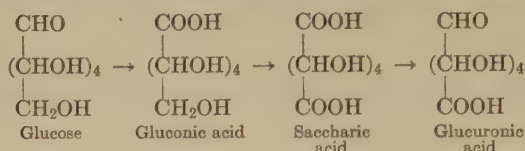


From the number of asymmetric carbon atoms in a compound, we can, with the help of a simple equation supplied by *van't Hoff*, calculate the possible number of isomers. The equation is $A = 2^n$, where A represents the number of isomers and n the number of asymmetric carbon atoms. Applying this equation to glucose, $A = 2^4 = 16$; there should be in all 16 possible stereoisomers. All of these have been isolated.

Glucose (both as a solid and in the form of syrup, as corn syrup) is used extensively in making confectionery, jellies, preserves, table syrups, in the manufacture of alcoholic beverages, as a diluent (to increase bulk and weight) for dyes, in chewing gum, tobacco, etc.

With bromine water glucose yields gluconic acid, which can be oxidized to saccharic acid by means of nitric acid. Heating saccharic

acid converts it into its lactone, which can then be reduced to glucuronic acid with sodium amalgam and dilute sulfuric acid:



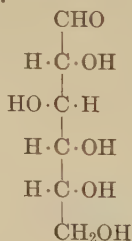
Gluconic acid is now made by the electrolytic oxidation of glucose and also by the action of *Penicillium luteum purpurogenum* on glucose. Calcium gluconate is used in calcium therapy.

Glucuronic acid is of importance physiologically, since it may combine with poisonous substances, such as phenol, chloral, etc., to make them inert (detoxication).

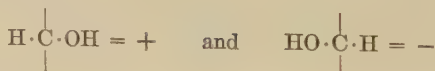
The Spatial Arrangement of Glucose. This is traced to glyceraldehyde, which may be written in two forms:



From each isomer of this aldehyde, eight isomers of glucose may be obtained (see the aldose chart). From *d*(+)-glyceraldehyde we arrive at *d*(+)-glucose (which is the common form of glucose).¹ It has the following spatial arrangement:



Using the notation that



then *d*(+)-glucose can be represented in shorthand form as



¹ It has been suggested that *D* and *L* be used instead of *d* and *l*, since they relate to structure and not sign of rotation.

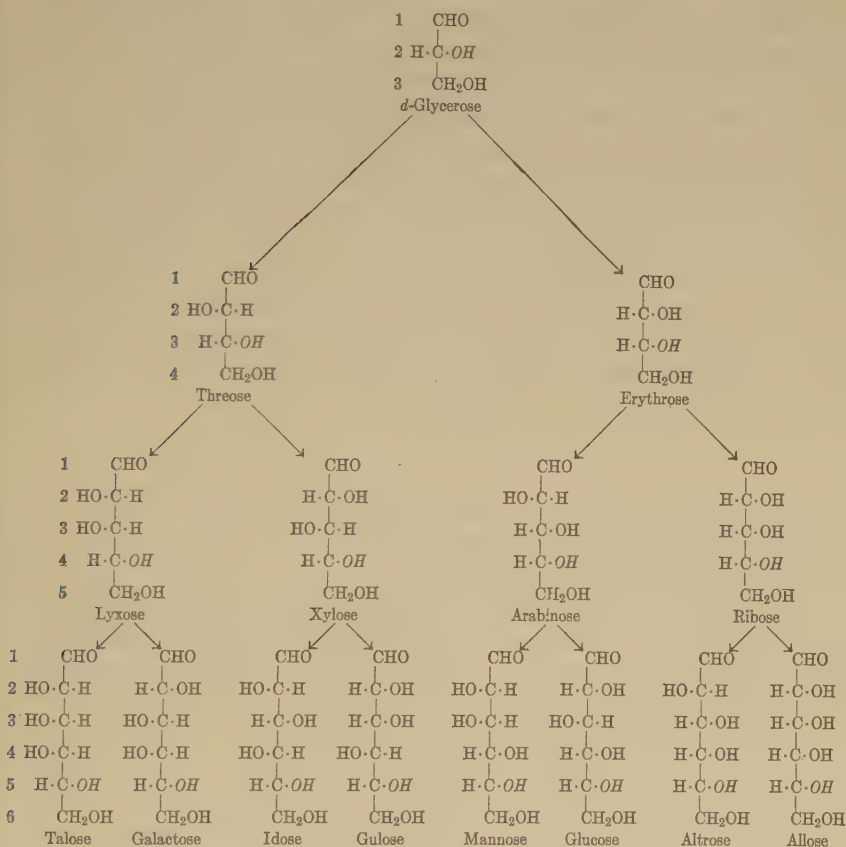
Here the two end-carbon combinations are ignored in the notation. We can represent the sixteen possible isomers as follows:



The first of each pair represents the *d* series (related to *d*-glucose and *d*-glyceraldehyde); and the second, the *l* series.

In this *d* series, the hydroxyl group next to the primary alcohol group always faces right, whereas in the *l* series that group always faces left.

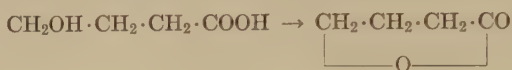
CONFIGURATION OF THE *d*-ALDOSES *



* Reprinted by permission from Harrow's *Biochemistry*, W. B. Saunders Co., 1943.

The Cyclic Structure of Glucose. The above formula is still not completely satisfactory. Glucose, for example, is pictured as an aldehyde;

but this is not altogether true. The common aldehydes give a positive Schiff test (the formation of a reddish violet color with magenta solution which has been decolorized with SO_2); but glucose does not give this test. Nor does glucose form stable addition compounds with sodium bisulfite, as the aldehydes do. Furthermore, the gamma and delta varieties of hydroxy acids tend to form lactones (p. 146), which converts them into cyclic compounds:



Some very convincing evidence for a similar structure for glucose, and this holds true of the other sugars, is obtained from a study of the *mutarotation* of glucose, "mutarotation" meaning a change of rotation. Glucose solution, freshly prepared, has a specific rotation of $+111^\circ$; but, when it stands, the rotation changes to $+52^\circ$. The specific rotation of a compound is a specific property of that compound, similar to such physical constants as boiling and melting points. Therefore, a change of rotation suggests a change in the structure of the compound.

The specific rotation, $[\alpha]$, is defined as the rotation of a solution containing 1 gram of substance per milliliter in a polarimeter tube 1 dm (decimeter) long at a specific temperature (ordinarily 20° or 25°) for monochromatic light, almost always sodium light (the D line of the visible spectrum) unless otherwise specified. The formula used generally is

$$[\alpha]_D^{t^\circ} = \frac{\alpha}{l \times c}$$

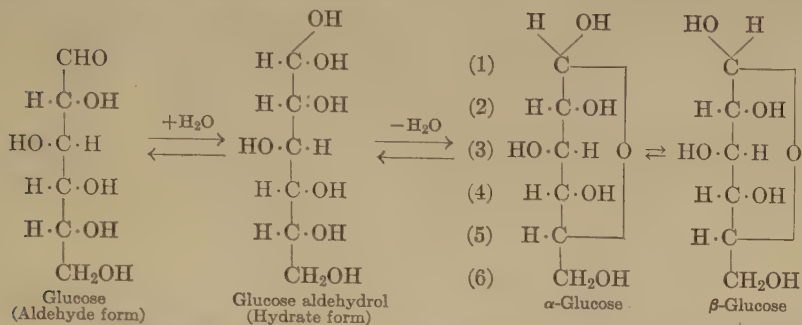
in which α = the observed rotation in angular degrees, l = length of the polarimeter tube in decimeters (usually 2), c = concentration of the solution in grams per milliliter.

The determination of specific rotation is a fundamental operation in sugar analysis. The "saccharimeters" used are special polarimeters in which ordinary white light is polarized by quartz, and the scale reads percentage of sugar (generally sucrose, the most common one).

Further evidence of the change in structure, as a result of mutarotation, is obtained when we take the glucose, with $[\alpha] +111^\circ$, dissolve it in boiling pyridine, and crystallize from this solvent. We now get a form of glucose with $[\alpha] +19^\circ$; but this, also, on standing, changes to $[\alpha] +52^\circ$. ($t = 20^\circ \text{C.}$)

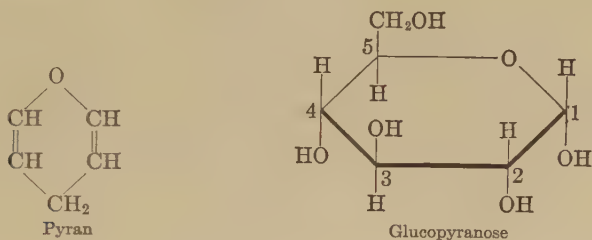
The glucose with an optical rotation of $+111^\circ$ is called α -glucose, and the one with a rotation of $+19^\circ$ is the β -modification. These changes in glucose may be explained by assuming the formation of two

lactone-like structures which exist in equilibrium with each other and with the "open" aldehyde form:



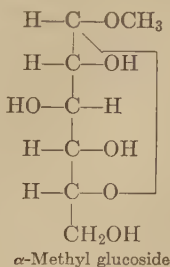
Carbon 1 is asymmetric in the cyclic formula and thus accounts for the two forms. This lactone-type structure may also be considered a hemiacetal of the aldehyde with the alcoholic group at carbon 5.

We have assumed a 1,5 oxygen bridge; and we shall presently give some evidence for this structure. But, assuming this to be true for the time being, glucose may also be looked upon as a derivative of pyran, glucopyranose:

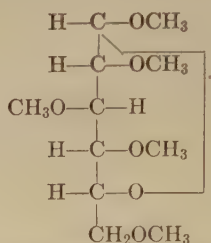


Haworth showed this model in perspective, with the H and the OH groups above or below the plane of the ring. The ring is at right angles to the plane of the paper. The thin bonds of the ring are behind the plane of the paper, and the thick bonds in front of it.

Methylation. When glucose is treated with methyl alcohol and hydrogen chloride, methyl glucosides are formed:

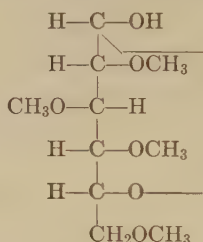


This methyl glucoside is next treated with dimethyl sulfate and methyl iodide in alkaline solution, which completes the methylation of the hydroxyl groups:

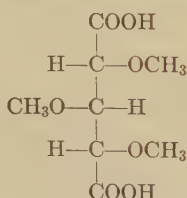


2,3,4,6-Tetramethyl- α -methyl glucoside

The methoxy group at carbon 1 can be easily hydrolyzed, but the other methoxy groups (ether groups) cannot. This means that upon hydrolysis we get



which can be called tetramethyl- α -glucopyranose. When this compound is oxidized with nitric acid we get trimethoxyglutaric acid:

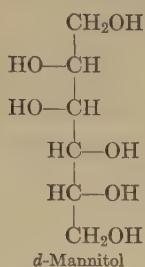
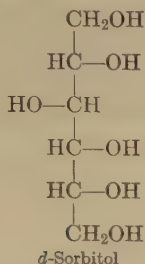


This is an indication that the oxygen atom is attached to carbon atom 5.

Fermentation. The enzyme *zymase*, which converts glucose into alcohol and carbon dioxide, does not function properly unless phosphates are present. These phosphates form combinations with glucose.

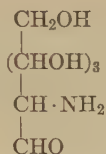
Still another substance that is necessary for proper fermentation is spoken of as a "cozymase," which, unlike *zymase*, is not destroyed by heat. This cozymase has been isolated and has been shown to consist of a combination of the purine adenine, the five-carbon sugar ribose, phosphoric acid, and the amide of nicotinic acid (p. 336).

By electrolytic reduction of glucose, two alcohols, *d*-sorbitol and *d*-mannitol, are produced:



Being hexahydric alcohols, they are used for the preparation of ethers, of esters, and of resins, etc. They are good humidifying agents. An example of the use of sorbitol is in a preparation of vitamin C, or ascorbic acid (p. 395).

Glucosamine,



a substance closely related to glucose, is an important constituent of glycoproteins, such as mucin, and may be obtained from mucin by hydrolysis. It is also present in chitin, a constituent of the shell of crustaceans and insects. Glucosamine reduces *Fehling's* solution, and its general properties are much like those of glucose.

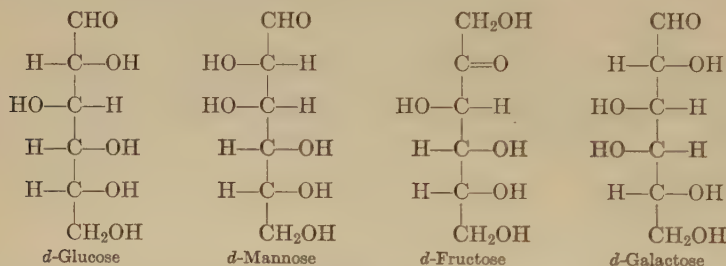
Galactose is an aldohexose. It is obtained by the hydrolysis of lactose or milk sugar. It is also an important constituent of the cerebrosides of the brain. Like glucose, it forms an osazone with phenylhydrazine (differing, however, in structure), and reduces *Fehling's* solution, but ferments slowly with yeast. On oxidation, it forms mucic acid (stereoisomer of saccharic acid), which also differentiates galactose from glucose.

Fructose, or levulose, or fruit sugar, found in honey, is a ketohexose, isomeric with glucose and galactose. Fructose, glucose, and galactose are, physiologically, the three important hexoses. Fructose may be obtained by hydrolysis of cane sugar or sucrose. Like the other two common hexoses, fructose reduces *Fehling's* solution and forms an osazone. The osazone with phenylhydrazine is the same as the one formed with glucose. It may be distinguished from glucose and galactose by the *Seliwanoff* test, which consists in heating fructose with resorcinol dissolved in dilute HCl, whereby a red color and a red precipitate are

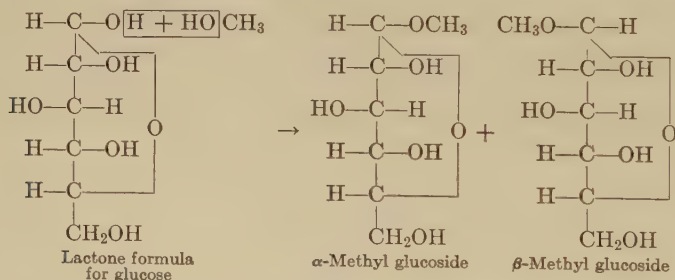
obtained. Fructose is 50 per cent sweeter than sucrose. A method has been proposed to prepare fructose in large quantities from the Jerusalem artichoke (p. 208).

i-Fructose, $C_6H_{12}O_6$, is obtained by polymerization of six moles of formaldehyde with calcium hydroxide. A mixture of sugars is obtained known as "formose" from which *i*-fructose has been isolated. *i*-Fructose is the racemic (*dl*) form.

The stereo-configurations of four of the hexoses can be shown by the following open-structure formulas:



Glucosides. When glucose reacts with methanol in presence of HCl, two compounds, α - and β -methyl glucosides, are obtained, the formulas of which may be represented thus:



The existence of the two isomeric glucosides is further evidence for the lactone-type formula.

The two glucosides have different physical properties. They also behave differently towards enzymes. Maltase hydrolyzes the α -variety, but not the β -, and emulsin hydrolyzes the β - but not the α -.

The naturally occurring glucosides belong to the β -form. On hydrolysis, glucose and other compounds are produced. Many glucosides occur in nature: phloridzin, found in the bark of fruit trees, yields fructose and phloroglucinol when hydrolyzed; phloridzin is often used to induce a form of diabetes in animals. Salicin, $C_6H_4 \begin{array}{l} \nearrow \text{O} \cdot C_6H_{11}O_5 \\ \searrow \text{CH}_2\text{OH} \end{array}$, on hydrolysis

yields glucose and saligenin, or salicyl alcohol; salicin occurs in willow bark. Amygdalin, $C_6H_5 \cdot CH \begin{cases} \text{CN} \\ \text{O} \cdot C_{12}H_{21}O_{10} \end{cases}$, hydrolyzes to two molecules of glucose, HCN and benzaldehyde; it is found in bitter almonds.

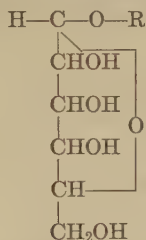
Arbutin, $C_6H_4 \begin{cases} \text{O} \cdot C_6H_{11}O_5 \\ \text{OH} \end{cases}$, hydrolyzes to glucose and hydroquinone;

it is present in the leaves of the berry tree. Indican, present in the indigo plant, hydrolyzes into glucose and indoxyl, which rapidly oxidizes to indigo. Myronic acid is present in black mustard seed; on hydrolysis, it is converted to glucose, $KHSO_4$, and allyl isothiocyanate ($C_3H_5 \cdot NCS$). Ruberythric acid is present in madder root; on hydrolysis or fermentation, it is converted to the dye alizarin and glucose.

Similar compounds of the other monosaccharides are generally called *glycosides*.

DISACCHARIDES, ETC.

Disaccharides may be regarded as glycosides



in which R represents another molecule of monosaccharide in which there may or may not be a potential aldehyde group represented by a glycosidic OH group, $\text{H}-\text{C}-\text{OH}$. With such a group, the disaccharide

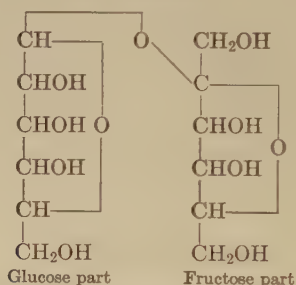


(and any other carbohydrate) is a reducing sugar; it reduces *Fehling's* solution, forms an osazone with phenylhydrazine, and exhibits mutarotation. Upon methylation, the glycosidic OH and the alcoholic OH groups form methoxy groups. Upon hydrolysis, the methylated disaccharide splits into two molecules of methylated monosaccharide; one of these contains the glycosidic OH which was regenerated by hydrolysis.

The present structures of disaccharides have been established on the basis of such reactions.

Sucrose, or cane sugar, $C_{12}H_{22}O_{11}$, is one of three physiologically important disaccharides, the other two being lactose and maltose. On

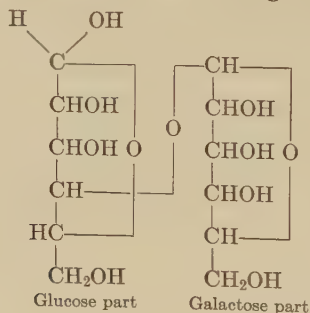
acid hydrolysis, sucrose yields a mixture of glucose and fructose ("invert sugar"). The same result is brought about by the enzyme *sucrase*, found in the small intestine. On a large scale, sucrose is obtained from sugar cane, sugar beet, etc. Unlike dextrose, fructose, galactose, maltose, and lactose, five other important sugars, it does not reduce *Fehling's* solution, nor does it form an osazone—that is, it is not a reducing sugar. To explain this, the suggested formula for sucrose does not contain a glucosidic hydroxyl group:



When sucrose is heated above its melting point, caramel is formed. This is a brown substance, and is used extensively as a coloring material in food preparations.

Whether the sugar is obtained from the sugar cane or the sugar beet, the extraction process consists in first separating the juice from the insoluble fiber, next in precipitating albuminous material and neutralizing the acids present, and finally in evaporating the filtrate and separating the crystals from the mother liquor. The mother liquor contains some 50 per cent of sucrose and is known as molasses, a product used in the making of alcohol. If the molasses is derived from the sugar cane, it may be used as table syrup and in the preparation of rum.

Lactose, $C_{12}H_{22}O_{11}$, or milk sugar, occurs in milk to the extent of about 4 per cent. On hydrolysis, or by the action of the enzyme *lactase* in the small intestine, it yields glucose and galactose. Since it is a reducing sugar, we assume that it contains a glucosidic hydroxyl group.



Maltose, $C_{12}H_{22}O_{11}$, or malt sugar, is found in malt, which is the sprouted grain of barley. This sprouted grain contains an enzyme, *diastase*, which converts the starch in the grain into maltose. A similar action occurs in the body when the enzyme *ptyalin*, found in saliva, acts on the starch in foods. When maltose is hydrolyzed by acids, or by *maltase* (an enzyme found in yeast and also in the small intestine), two molecules of glucose are obtained. The *maltase* in yeast, acting on maltose, forms glucose, and then the *zymase* in yeast, acting on glucose, produces ethyl alcohol and carbon dioxide. Maltose behaves similarly to lactose, but the lactose forms galactose as one of its products of hydrolysis, whereas maltose forms only glucose. Maltose is a reducing sugar.

Raffinose, $C_{18}H_{32}O_{16}$, is a trisaccharide occurring in cottonseed, etc. It does not reduce *Fehling's* solution. On hydrolysis, it yields fructose, glucose, and galactose. This hydrolysis may be brought about either by acids or by certain bacteria and yeasts.

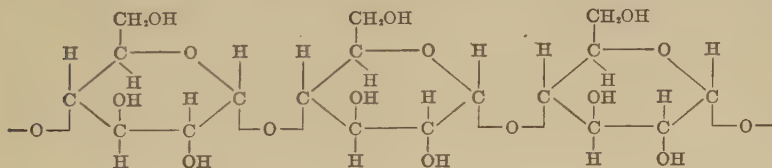
Chitin, a tetrasaccharide, is probably composed of four glucosamine (p. 203) units. It is prepared from the shells of lobsters or crabs.

Chondroitin, another tetrasaccharide, is contained in cartilage, often in combination with protein.

POLYSACCHARIDES

Starch, one of a number of polysaccharides having the general formula $(C_6H_{10}O_5)_x$, is widely distributed in the vegetable kingdom. It is synthesized in the plant by the combined action of carbon dioxide and water in the presence of chlorophyll. It is hydrolyzed in the body first to soluble starch, then to a number of dextrans, then to maltose, and finally to glucose, in which form it is absorbed into the blood stream. Boiled with water, the granules swell and burst, and "starch paste" is obtained. Starch gives a blue color with iodine.

Starch can be represented as a condensation polymer of α -glucose:



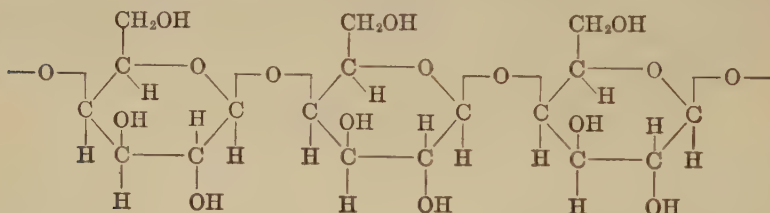
Dextrans of the general formula $(C_6H_{10}O_5)_x$ are considered somewhat less complex than starch itself, for the dextrans are obtained in the course of the hydrolysis of starch by enzymes. Erythrodextrin gives a reddish brown color with iodine, and achrodextrin fails to give any color.

Glycogen, or "animal starch," $(C_6H_{10}O_5)_x$, is found almost exclusively in animals, and particularly in the liver. It is the form in which carbohydrate is stored in the body. With iodine it gives a red color.

Inulin is a polysaccharide found in the tubers of the Jerusalem artichoke, dahlia, etc. Unlike starch, it is soluble in hot water and gives a negative reaction with iodine. On hydrolysis, it yields the monosaccharide fructose.

Cellulose, $(C_6H_{10}O_5)_x$, is the chief constituent of the cell wall of plants. Cotton fiber is almost pure cellulose, or "normal" cellulose. When hydrolyzed, cellulose yields glucose. This reaction has been used to make cattle feed from wood, and also ethyl alcohol by fermentation of the sugar obtained by hydrolysis. Lignocellulose is probably a combination of cellulose with gums and resins; pectocellulose is a combination of cellulose and a substance, pectin, which is responsible for the formation of jellies from fruit.

It has been suggested that the cellulose molecule may be represented as a polymer of β -glucose:



Cellulose is, chemically, highly inert. It may be dissolved (possibly with some changes) in *Schweitzer's* reagent (ammoniacal solution of copper oxide).

Acetyl derivatives may be obtained with glacial acetic acid and with acetic anhydride, showing cellulose to contain OH groups.

Industrially, cellulose is of immense importance. It is the chief ingredient of cotton, linen, hemp, etc., and of paper (which, in turn, may be made from cotton and linen rags or from wood). Parchment paper is cellulose treated with concentrated sulfuric acid. Mercerized cotton is cotton treated with sodium hydroxide solution, whereby the cotton is converted into a stronger fiber with a glossy appearance somewhat resembling silk. It takes dyes more readily than cotton.

Rayon, or, as it was called for a time, *artificial silk*, is manufactured in one of four different ways. In the *nitrocellulose process* (now used very little), the cotton linters are treated with a mixture of nitric and sulfuric acids, and the nitrocellulose (cellulose nitrate) so obtained is dissolved in alcohol and ether. The solution is then forced by pressure

through capillary-type tubes, and, by the application of blasts of hot air, the filaments which form solidify. These filaments are still nitro-cellulose in composition and highly flammable. The nitro group is therefore removed by treatment with sodium hydrosulfide. In the *cuprammonium process*, the linters or wood pulp are mixed with copper hydroxide and the mixture is dissolved in concentrated ammonia. The solution is forced through fine holes into a bath of caustic soda or sulfuric acid, thereby causing the filaments to coagulate. In the *acetate process* the linters are treated with acetic anhydride, glacial acetic acid and sulfuric acid also being present. The cellulose acetate so formed is precipitated with water and dissolved in acetone. The viscous solution is now forced under pressure through the capillary tubes to produce the fine filaments which, when spun in groups and twisted, result in a yarn known in the trade as Celanese and Lustron. Unlike the other varieties of rayon, which are really pure cellulose, this product is really cellulose acetate.

Cellulose acetate is more stable to heat and light than cellulose nitrate. The acetate is now extensively used in the manufacture of non-flammable photographic films, cellulose plastics, non-shatterable glass, phonograph records, lacquers, transparent wrappers, etc.

The method most commonly used in the preparation of rayon (or cellophane) is the *viscose process*, a process by which 80 per cent of the total world's production of rayon is made. Spruce pulp or cotton linters are soaked in an 18 per cent caustic soda solution, thereby causing a swelling of the fibers and the production of a compound known as soda cellulose. The soda cellulose is next treated with carbon disulfide, forming a product known as cellulose xanthate, which, unlike the cellulose, is a water-soluble compound, and is known as "viscose." The solution is forced through fine holes into sulfuric acid, the filaments so formed consisting of regenerated cellulose. For cellophane the cellulose is extruded into sheets. As in the other three processes, the filaments are finally converted into skeins of twisted yarn. Here, again, the skeins are bleached with chlorine. In the viscose process, sulfur impurities arising from the use of carbon disulfide are removed by treatment with sodium sulfide prior to bleaching with chlorine.

Within a generation rayon has taken a commanding place in the textile industry and is finding applications in all phases of the textile trade.

With nitric acid, cellulose forms various nitrate compounds. The higher nitrates (hexanitrate), such as guncotton (gelatinizes in alcohol-ether mixture), are explosives; and the lower nitrates are used in the manufacture of celluloid. Pyroxylin, a mixture of lower cellulose

CHEMICAL PRODUCTS OF CELLULOSE

COTTON 1,2				WOOD 2						
ESTERS AND GELS				CHEMICAL PULPS						
DECOMPOSITION PRODUCTS				MECHANICAL PULP 4						
Nitrate	Acetate	Viscose	Cuprammonium	Hydrolysis	Alkali fusion	Distillation 6	Sulfite 1 pulp	Soda 2 pulp	Sulfate pulp	Groundwood
Artificial silk Films Lacquers Plastics Explosives	Artificial silk Films Lacquers	Artificial silk Films	Artificial silk	Alcohol Cattle food Acetic acid Furfural	Oxalic acid Pyrocatechol 5 Protocatechuic acid 6 Acetic acid 6	Methanol "Methyl acetone" Formaldehyde Acetic acid Acetone Methyl ethyl ketone Acetone oils Charcoal Tar Pitch Creosote	Writing 3 Tissue Wrapping	Book Blotting	Wrapping "Kraft"	Newsprint Wall
									See Note 7	

See Note 7

1. Sulfite pulp is used in place of cotton to some extent especially in making the viscose products.
2. Cotton linters are used for making certain paper pulps similar to the soda wood pulp.
3. Rags are used alone or in mixture with sulfite pulp in high-grade writing papers.
4. Mechanical pulp is, of course, not a chemical product, but its manufacture and use are so closely connected with the chemical pulp, especially sulfite pulp, that it is included here for completeness.
5. Oxalic acid is the only product that has been made commercially by the alkali fusion of wood.
6. Resinous wood distillation products are not included here because they are very largely products of the resin in the wood and not of the fiber.

7. The papers mentioned here are only those that are made to a very large extent from the particular kind of pulp under which they are arranged. There are many different kinds of papers, but they cannot be readily arranged on this chart since they may be made up of so many different combinations of pulps. Following are some of these combinations:

Sulfite (A)	Soda (B)	Sulfite (C)	Groundwood (D)
Newsprint	A and D	A and D	
Book and magazine	B, A, and B; A, B, and D		
Writing	A, A and rag paper		
Wrapping	A, C, A and D, C and D		
Tissue	A, A and D		
Blotting	B		
Glossine	A		
Board	D, A, C, and old paper in various mixtures		
Wall	D, D and A, D and C		
Bag	A, C, A and D, C and D		

nitrates, is used in preparing lacquers and making rayon and celluloid. It is soluble in amyl acetate and methanol, and in acetone; and in a mixture of 3 volumes of ether and 1 volume of ethyl alcohol, it forms the pharmaceutical product known as "collodion." Pyroxylin contains 10.5–12.2 per cent and guncotton about 13.4 per cent of nitrogen.

An important product containing pyroxylin, known under the name "Duco," is used very extensively as a lacquer finish. The pyroxylin is dissolved in amyl acetate or other solvents, and small amounts of gums or resins are added, producing a lacquer. By the addition of finely ground pigments, pyroxylin enamels are produced. When a lacquer film is exposed to the air the solvents, which have acted as a vehicle for the pyroxylin, gums, pigments, immediately begin to evaporate, and in a short time a hard, tough film is produced. Linseed oil and other vegetable oil paints dry by air oxidation, whereas the pyroxylin lacquers dry entirely by evaporation. Collodion, similar to pyroxylin in composition, is used for photographic films, as a protective covering for wounds, etc., and in the making of dialyzing bags. Celluloid is made by subjecting pyroxylin and camphor to heat and pressure. Cordite, a smokeless powder, is made by treating guncotton and nitroglycerin with acetone and some vaseline.

When alkali cellulose and ethyl chloride react, the ethyl ether of cellulose is formed. Being an ether, it resists attack by alkalis and dilute acids. The commercial product is known as "ethyl cellulose." It is used in the manufacture of coating compositions, films, and plastics.

Mannans, Galactans, Hemicellulose, Etc. These substances, present in the seeds of numerous plants, resemble cellulose, but dissolve in dilute alkali and on hydrolysis yield not only glucose (as cellulose does) but other hexoses as well. Agar-agar is a galactan which yields galactose on hydrolysis. Mannans, as their name implies, yield mannose when hydrolyzed.

Gums, Pectins, Mucilages. These are also polysaccharides containing pentose and hexose groups. The gums are probably carbohydrates combined with acids. Some are soluble, and others insoluble, in water. Gum arabic, gum tragacanth, etc., are used as vehicles to suspend insoluble substances in aqueous emulsions. Mucilages form viscous liquids with water. The gelatinization of fruit extracts is due to the pectin present.

QUESTIONS

1. Write the configuration of an aldotetrose which on oxidation would produce optically active dicarboxylic acids.
2. Calculate the amount of acetic anhydride necessary to acetylate completely 1 gram of crystalline glucose ($C_6H_{12}O_6 \cdot H_2O$).

3. Write structural formulas for the following: (a) glucose oxime; (b) glucuronic acid; (c) *d*(+)-glyceraldehyde; (d) α -methyl glucoside; (e) fructose.
4. Indicate the chemical composition of the following: (a) invert sugar; (b) pyrox-
ylin; (c) collodion; (d) mercerized cotton; (e) parchment paper; (f) ethyl
cellulose; (g) viscose; (h) cellulose acetate; (i) glycogen; (j) pentosan;
(k) *Fehling's* solution; (l) *Schweitzer's* reagent; (m) glucoside; (n) cellulose;
(o) smokeless powder; (p) celluloid; (q) cellophane; (r) rayon; (s) dextrin.
5. Write equations for the preparation of the following compounds:

(a) phenylglucosazone	from glucose
(b) phenylglucosazone	" fructose
(c) fructose	" glucose
(d) sucrose octaäcetate	" sucrose
(e) fructose and glucose	" sucrose
(f) glucose	" maltose
(g) glucose	" starch
(h) an aldotetrose	" an aldopentose
(i) an aldopentose	" an aldotetrose
(j) gluconic acid	" glucose
(k) saccharic acid	" glucose
6. Calculate the percentages of α - and β -glucose present at equilibrium in a solu-
tion of glucose at 20° C.
7. Maltose after methylation and hydrolysis yields 2,3,4,6-tetramethyl glucose and
2,3,6-trimethyl glucose. It is a reducing sugar. Write a possible structure
for maltose.
8. If 25 ml of a 0.1 *M* water solution of sucrose in a 2-dm polarimeter tube gave a
reading of +4° 33' at 25° C for sodium (D) light, calculate the specific rota-
tion of sucrose.

CHAPTER XVIII

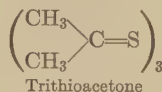
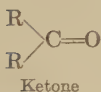
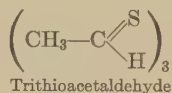
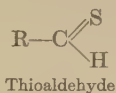
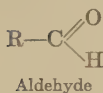
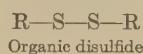
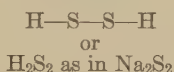
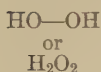
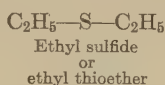
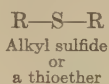
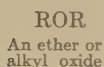
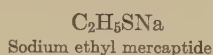
SULFUR, PHOSPHORUS, ARSENIC, AND ORGANO-METALLIC COMPOUNDS

SULFUR COMPOUNDS

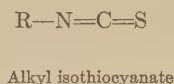
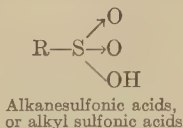
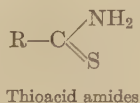
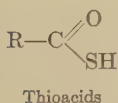
Sulfur is just below oxygen in the periodic table, and the two elements should, therefore, show close relationships. We find abundant evidence of such structural relationships in organic chemistry. An entire series of analogous compounds may be formed by substituting sulfur for oxygen in organic compounds.



These are called mercaptans because they form insoluble mercury salts (*corpus mercurium captans*).



In addition to these types of compounds we have:



and others, each of these sulfur compounds showing a close analogy to the corresponding oxygen compound.

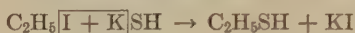
Many of these sulfur compounds may be prepared from their oxygen analogs by the use of phosphorus pentasulfide, even though the yields are poor; e.g.,



Most of the compounds having the structure $\text{R}-\text{S}-\text{H}$ and $\text{R}-\text{S}-\text{R}$ have exceedingly putrid, disagreeable odors and are poisonous.

Mercaptans may be prepared:

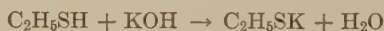
1. By the action of potassium hydrogen sulfide on an alkyl halide:



2. On a large scale, by the action of H_2S on alcohols in the presence of a catalyst:



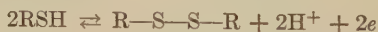
Mercaptans are converted to mercaptides thus:



Ethyl mercaptan, $\text{C}_2\text{H}_5\text{SH}$, and amyl mercaptan, $\text{C}_5\text{H}_{11}\text{SH}$, are used as warning agents in toxic gases.

On oxidation with HNO_3 or KMnO_4 , $\text{R}-\text{S}-\text{H}$ becomes $\text{R}-\text{S} \begin{array}{l} \nearrow \text{O} \\ \searrow \text{OH} \\ \searrow \text{O} \end{array}$, an alkanesulfonic acid.

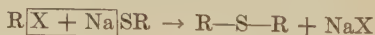
More gentle oxidation (O_2 , I_2) produces disulfides, which can be reduced back to thioalcohols and which can thus form a reversible oxidation-reduction system:



In biological oxidations, glutathione (p. 173) is thought to be an oxidation-reduction system of this kind.

Sulfides may be prepared:

1. By the action of a thioalkoxide on a halide:



Analogous to $\text{R}[\text{X} + \text{Na}]\text{OR} \rightarrow \text{ROR}$ (an ether) + NaX (*Williamson*)

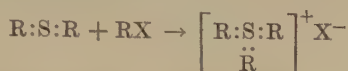
2. By the action of potassium sulfide on a halide:



The thioethers on oxidation (HNO_3 or KMnO_4) give, first, $\text{R}-\text{S} \begin{array}{l} \nearrow \text{O} \\ \searrow \text{R} \end{array}$,

sulfoxides, and then $\text{R} \begin{array}{l} \nearrow \text{S} \nearrow \text{O} \\ \searrow \text{S} \searrow \text{O} \end{array}$, sulfones.

Sulfur, like oxygen and nitrogen, is capable of forming "onium" compounds by contributing electrons to form coordinate covalences. Sulfides or thioethers (compare ethers, p. 77) form sulfonium compounds by addition of alkyl halides:

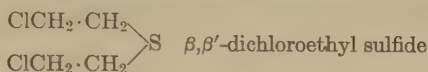


Hydrolysis of these sulfonium halides with silver oxide, for instance, yields sulfonium hydroxides, which are strong bases:

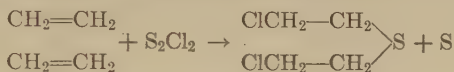


Mercaptans, sulfides, disulfides, etc., occur in petroleum.

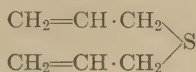
Mustard gas (one of the most toxic gases used in war) is



It is manufactured by passing ethylene into sulfur monochloride,

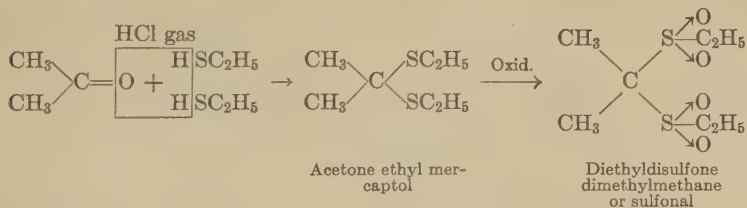


Oils of garlic and onion contain allyl sulfide:



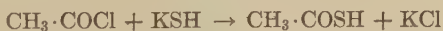
When ethylene dichloride, $\text{CH}_2\text{Cl}-\text{CH}_2\text{Cl}$, is reacted with sodium polysulfide, and the resulting product is polymerized, a rubberlike substance is produced. This is known as "Thiokol A."

Sulfonal may be prepared from acetone by combining it with ethyl mercaptan in the presence of a dehydrating agent and oxidizing the product with KMnO_4 :



Sulfonal and trional (the ethyl methyl analog) are used as hypnotics.

Thioacetic acid or ethanethiolic acid, CH_3COSH , is prepared by the following reaction:



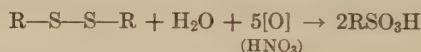
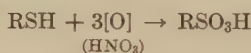
Sulfoacetic acid is $\text{CH}_2 \begin{matrix} \nearrow \text{SO}_3\text{H} \\ \searrow \text{COOH} \end{matrix}$.

Trithioacetaldehyde $\left(\text{CH}_3 - \text{C} \begin{matrix} \nearrow \text{S} \\ \searrow \text{H} \end{matrix} \right)_3$ and **trithioacetone**

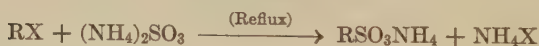
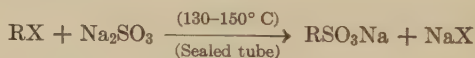
$\left(\text{CH}_3 \begin{matrix} \nearrow \\ \searrow \end{matrix} \text{C} = \text{S} \right)_3$ are prepared by the action of H_2S on acetaldehyde and acetone, respectively.

The alkanesulfonic acids (or alkyl sulfonic acids) of the type $\text{R}-\text{S} \begin{matrix} \nearrow \text{O} \\ \searrow \text{OH} \end{matrix}$ are used in the manufacture of detergents, drugs, and textiles. Two methods for their preparation are:

1. The oxidation of a mercaptan or a disulfide with nitric acid:



2. The action of a halide on a sulfite:



The salts of the higher members, C_8 through C_{18} , show the properties of soaps.

Taurine, or β -aminoethanesulfonic acid, $\begin{matrix} \text{CH}_2-\text{NH}_2 \\ | \\ \text{CH}_2-\text{S} \begin{matrix} \nearrow \text{O} \\ \searrow \text{OH} \end{matrix} \end{matrix}$, is a constituent

of taurocholic acid, which in the form of its sodium salt is an important constituent of the bile.

Xanthic acid, $\text{C} \begin{matrix} \nearrow \text{SH} \\ \searrow \text{OC}_2\text{H}_5 \end{matrix} = \text{S}$, is the ethyl ester of dithiocarbonic acid.

Sodium cellulose xanthate $\left(\text{C} \begin{matrix} \nearrow \text{SNa} \\ \searrow \text{O cellulose} \end{matrix} = \text{S} \right)$ is produced when cellulose is treated with CS_2 and NaOH solution. This is the basis for the viscose process (p. 209). **Thiourea**, $\text{C} \begin{matrix} \nearrow \text{NH}_2 \\ \searrow \text{NH}_2 \end{matrix} = \text{S}$, is the sulfur analog of urea,

$\begin{array}{c} \text{NH}_2 \\ \diagup \\ \text{C}=\text{O} \\ \diagdown \\ \text{NH}_2 \end{array}$, which in turn is the principal nitrogen end product in the metabolism of proteins in the body. Allyl isothiocyanate,



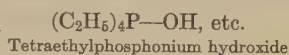
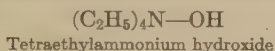
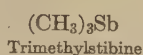
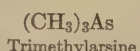
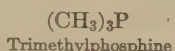
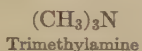
is present in mustard oil.

PHOSPHORUS AND ARSENIC COMPOUNDS

According to the periodic table, nitrogen, phosphorus, arsenic, and antimony belong to the same family of elements. This implies that compounds of P, As, and Sb, analogous to N compounds, should exist. These do exist. We have, for example, in inorganic chemistry:

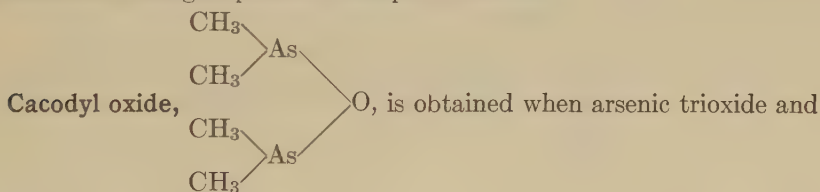


and in organic chemistry:



The phosphorus compounds are, as a rule, more reactive than the corresponding nitrogen compounds.

A number of proteins, such as the nucleoprotein found in the nuclei of cells, the casein in milk, and the phosphatides—of which the lecithin of egg yolk and brain tissue is an example—contain the element phosphorus as an integral part of a complex molecule.



potassium acetate are distilled:



The name **cacodyl**, "stinking," was given to the group $(\text{CH}_3)_2\text{As}$ by *Bunsen*, its discoverer. The cacodyl compounds are highly poisonous.

The salts of cacodylic acid, $(\text{CH}_3)_2\text{As} \begin{array}{c} \diagup \text{O} \\ \diagdown \text{OH} \end{array}$, such as sodium, calcium,

iron, and mercury cacodylates, are used in the treatment of syphilis, tuberculosis, malaria, and pellagra.

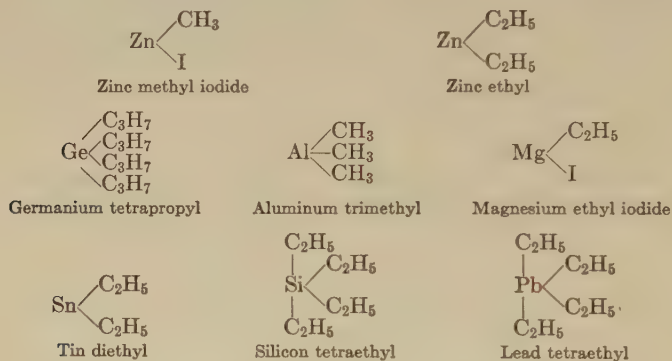
Ethyl dichloroarsine, $\text{C}_2\text{H}_5\text{AsCl}_2$, and chlorovinyl dichloroarsine, $\text{CH}=\text{CH}\cdot\text{AsCl}_2$, known as "Lewisite," are war gases.

Cl

The antimony compounds are similar in structure to those of arsenic. A number of very important arsenic compounds will be discussed in the aromatic series (p. 369).

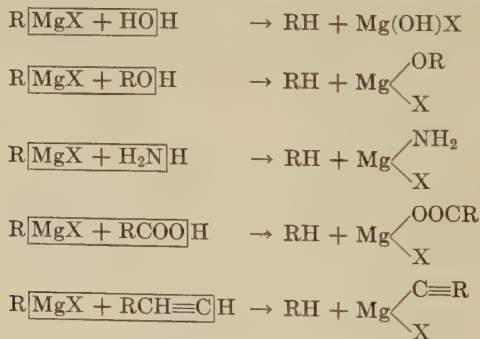
ORGANOMETALLIC COMPOUNDS

Various combinations of organic radicals with metallic elements are known. The following are examples:

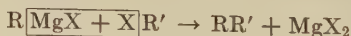


Compounds of the type $\text{R}-\text{Mg}-\text{X}$, **Grignard reagents**, are highly important since they are used extensively in organic chemistry. The reactions of these remarkably versatile compounds may be grouped into four general categories:

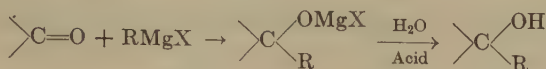
(a) Reactions with compounds containing an active hydrogen.



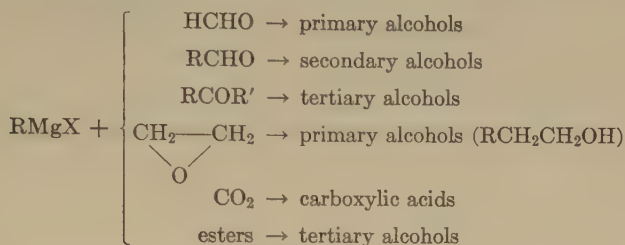
(b) Reaction with halides, saturated or unsaturated.



(c) Additions to carbonyl and similar compounds.

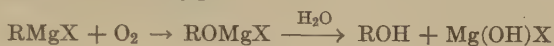


Under this heading, we can summarize some reactions which have already been explained:



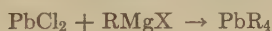
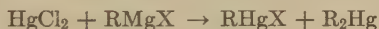
Compounds like the cyanides and acyl chlorides react similarly.

(d) The reaction with oxygen.

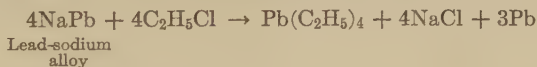


This reaction, as well as the reactions involving moisture (a) and halides (b), accounts for decrease of the yields in *Grignard* syntheses.

Inorganic halides undergo double decomposition to yield various other types of organometallic compounds; for example,



Lead tetraethyl, which is used as the "anti-knock" compound in automobile engines, is made commercially by the following method:



The product sold as "ethyl gas" is gasoline containing a small quantity of lead tetraethyl, ethylene dibromide, and ethylene dichloride.

Some of the organo-silicon compounds polymerize to yield *silicones*, which are more heat-resisting (lubricants, insulators) than carbon

polymers. Silicones have the general formula $\left(\begin{array}{c} \text{R} \\ \diagup \\ \text{---Si---O---} \\ \diagdown \\ \text{R} \end{array} \right)_n$.

QUESTIONS

1. Give the (a) name, (b) formula, and (c) method of preparation of one member of each of the following types of compounds: (1) mercaptans; (2) thioethers; (3) thioketones; (4) sulfones; (5) sulfonic acids.
2. Write structural formulas for the following compounds: (a) methyl mercaptan; (b) sodium thioethoxide; (c) ethyl sulfide; (d) diethyl disulfide; (e) thiopropionic acid; (f) dithiobutyric acid; (g) thiopropionamide; (h) methyl isothiocyanate; (i) sodium ethanesulfonate; (j) dimethyl sulfoxide; (k) dimethyl sulfone; (l) β, β' -dichloroethyl sulfide; (m) α, α' -dichloroethyl sulfide; (n) sulfonal; (o) trional; (p) thiourea; (q) sulfoacetic acid; (r) xanthic acid; (s) vinyl sulfide; (t) allyl sulfide; (u) allyl isothiocyanate; (v) triethylarsine; (w) triethylstibine; (x) cacodyl oxide; (y) ethyl dichloroarsine; (z) chlorovinyl dichloroarsine; (aa) zinc ethyl; (ab) lead tetraethyl; (ac) *n*-butyl magnesium iodide; (ad) mercury diethyl.
3. Describe the following syntheses:

(a) ethyl mercaptan	from ethyl alcohol
(b) methane	" methyl magnesium iodide
(c) ethyl hydrogen sulfate	" ethyl alcohol
(d) ethyl sulfide	" ethyl alcohol
(e) methyl ethyl sulfide	" methyl chloride
(f) dimethyl sulfone	" methyl iodide
(g) β, β' -dichloroethyl sulfide	" ethylene
(h) thioacetic acid	" acetic acid
(i) sulfonal	" acetone
(j) cellulose xanthate	" cellulose
(k) thiourea	" ammonium thiocyanate
(l) cacodyl oxide	" arsenic trioxide
(m) lead tetraethyl	" ethyl chloride
(n) isobutyl alcohol	" methanol and isopropyl alcohol
(o) <i>ter</i> -butyl alcohol	" methanol and isopropyl alcohol
(p) triethyl carbinol	" ethanol

From now on compare the following chapters with the corresponding ones in the aliphatic series.

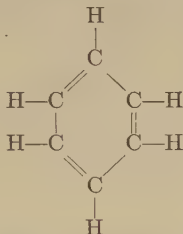
CHAPTER XIX

INTRODUCTION TO CYCLIC COMPOUNDS

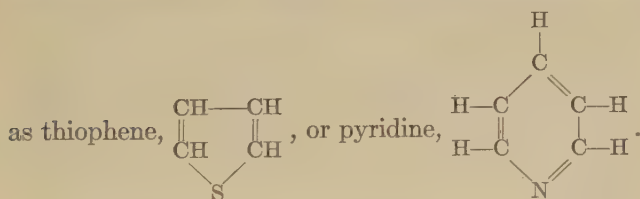
So far we have been studying the open-chain, or aliphatic, series of compounds. Now we are about to take up the closed-chain or cyclic compounds, which in many respects possess properties differing from those of the aliphatic series.

The cyclic compounds may be subdivided into two main divisions:

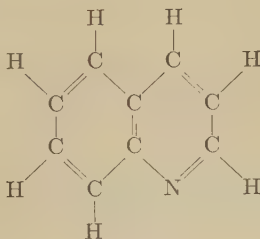
I. **Carbocyclic (isocyclic) compounds**, containing a ring of carbon atoms, such as benzene, for example,



II. **Heterocyclic compounds**, containing a ring which, in addition to carbon atoms, may contain one or more atoms of other elements, such



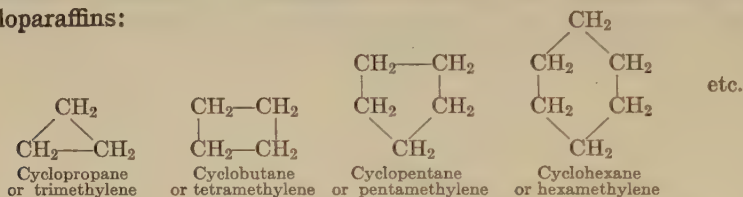
Combinations of carbocyclic and heterocyclic rings are also possible; for example, quinoline,



We have seen how the aliphatic series of compounds can be divided into typical groups, such as hydrocarbons, alkyl halides, alcohols, and ethers, and how the members of any one group show certain common characteristics which distinguish them from members of another group. Such typical divisions can also be made in the cyclic series, and here, to a certain extent, we find a series of compounds strictly analogous to those in the aliphatic series. Many of the type reactions which we shall consider in the following pages are those with which the student is already familiar.

ALICYCLIC COMPOUNDS

We have seen how the hydrocarbons of the aliphatic series can be classified into paraffins, C_nH_{2n+2} ; olefins, C_nH_{2n} ; and acetylenes, C_nH_{2n-2} . A series of compounds isomeric with the olefins are the **cycloparaffins**:

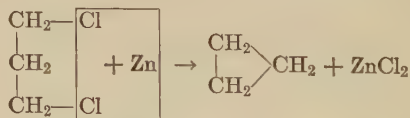


They are usually referred to as **alicyclic** compounds. As some of them occur in significant amounts in petroleum, they are also known as **naphthenes**.

The cycloparaffins can be prepared by two general types of reactions:

1. The *cyclization* of open-chain compounds. In general, any method of joining two carbon atoms—for example, the *Wurtz* synthesis or the *Grignard* syntheses—produces a ring structure if these two carbon atoms are at the two ends of a chain.

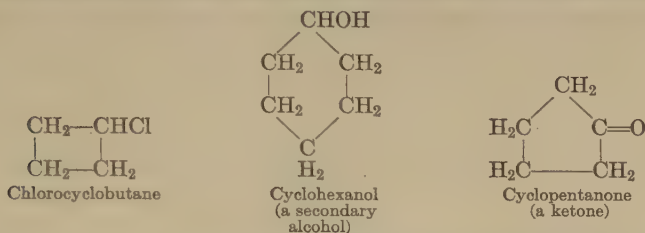
For instance, cyclopropane, an important anesthetic, is prepared by chlorinating propane to yield 1,3-dichloropropane (besides other chlorinated propanes), which is converted to cyclopropane by the use of zinc dust:



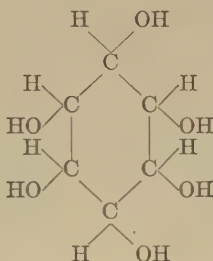
2. The *hydrogenation* of corresponding aromatic structures (p. 240). The abundance and variety of such aromatic compounds make this a very useful approach. The reduction products are also known as *hydroaromatic compounds*. Conversely, it is possible to dehydrogenate hydroaromatic compounds to aromatic substances by means of the usual hydrogenation catalysts or with S or Se.

Unlike the olefins, these compounds are not readily oxidized by potassium permanganate, and they usually form substitution rather than addition products. (Cyclopropane does add bromine, the ring opening to form 1,3-dibromopropane.) They cannot, therefore, be represented as double-bond compounds. In fact, they rather resemble the paraffins; and their name *cycloparaffins* is derived from that fact.

The cycloparaffins yield a series of derivatives comparable to those of the aliphatic hydrocarbons and with similar properties; for example:

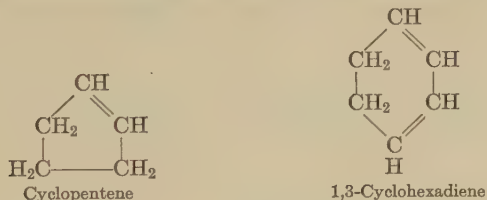


A derivative of cyclohexane (hexahydrobenzene) is hexahydroxyhexahydrobenzene, or inositol, a member of the vitamin B complex (p. 393):



Inositol is found in muscle and other animal organs, and in various fruits and vegetables. Its empirical formula is $\text{C}_6\text{H}_{12}\text{O}_6$ (compare with sugars), and it has often been called a cyclic sugar, though in reality it possesses none of the common properties of the sugars.

Cycloölefins are also known and are fully described by their names:



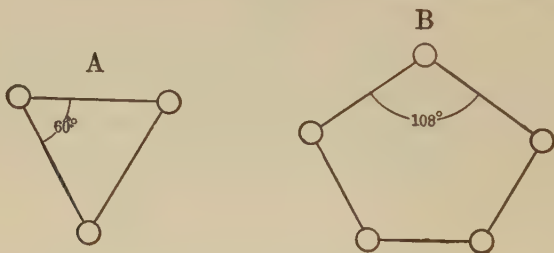
(From this point of view, benzene could be called 1,3,5-cyclohexatriene. This name is not used, since benzene and its homologs, as we shall see, bear little chemical resemblance to olefins, cyclic or acyclic.)

The various types of isocyclic structures described so far are often called **alicyclic** to denote their *aliphatic* behavior and *cyclic* structure, and also to distinguish them from the aromatic compounds, a much bigger and better-known category of cyclic compounds.

Stability of Ring Structures. Cyclic compounds containing five or six carbon atoms are more stable than those containing four and three carbon atoms. In the tetrahedral carbon atom, in which the four bonds, representing the four valences, radiate from the center to the corners of the tetrahedron, the angle between any two bonds is $109^{\circ} 28'$.



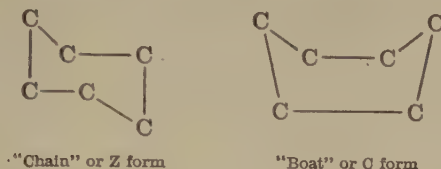
When two atoms unite, the connecting bond may be represented as a straight line between these atoms. In a ring containing three carbons, the picture may be viewed as shown in A. Here the angle between the valence bonds is 60° in the place of $109^{\circ} 28'$, bringing about a great "strain" and the probability of a relatively unstable compound. In a five-carbon ring, as shown in B, the angle between the valence bonds approaches that seen in the tetrahedral carbon model itself, and the "strain" is no longer present, which makes for a relatively stable compound. This explanation is referred to as *Baeyer's strain theory*.



From the same point of view, the olefinic double bond is a two-carbon cycle, in which the strain is the greatest possible; this corresponds to the unusually high reactivity of the olefins.

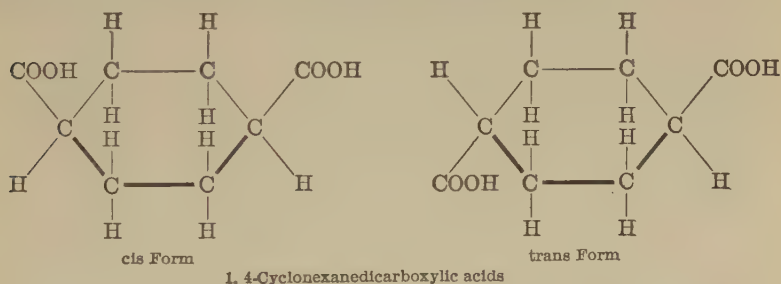
In a six-, seven-, eight-, etc., carbon ring a "strain" is produced in the opposite direction to that represented by three- and four-carbon rings. Many such compounds, however, are quite stable. As a matter of fact, compounds with as many as 34 carbon atoms in one ring have been made. *Baeyer's* explanation is apparently untenable for rings of more than five

carbon atoms; but then he assumed uniplanar rings in which, of course, strains would be set up. If, however, we build tetrahedral carbon models of these cyclic structures, we see that "puckered" models, with the carbons in more than one plane, exist in a strainless condition. For cyclohexane, for example, we can get two stable models of this type:

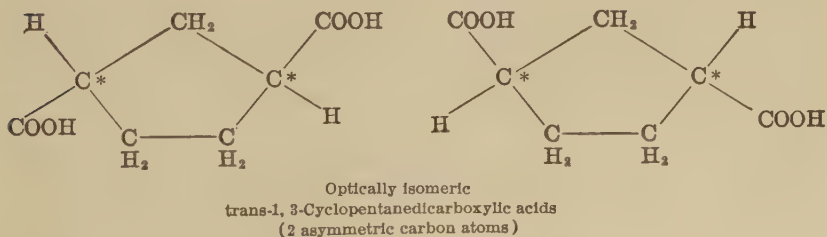


There is some experimental evidence for the existence of two such forms, as well as for the existence of several strainless ring forms of other cyclic structures.

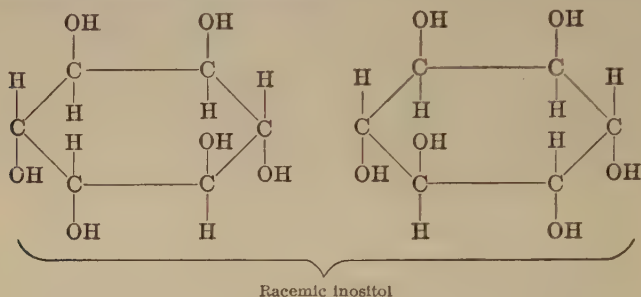
We have already seen that the existence of geometrical isomers is explained on the basis of restricted rotation about a double bond or two-carbon cycle. It is therefore easy to account for similar examples of geometrical isomerism with larger rings; the two carbons involved are separated by a larger cycle which restricts rotation too:



As a matter of fact, some *trans* forms have structures with non-superposable mirror images, that is, asymmetric molecules. This corresponds with the fact that many such structures have been resolved into the *d* and *l* forms:

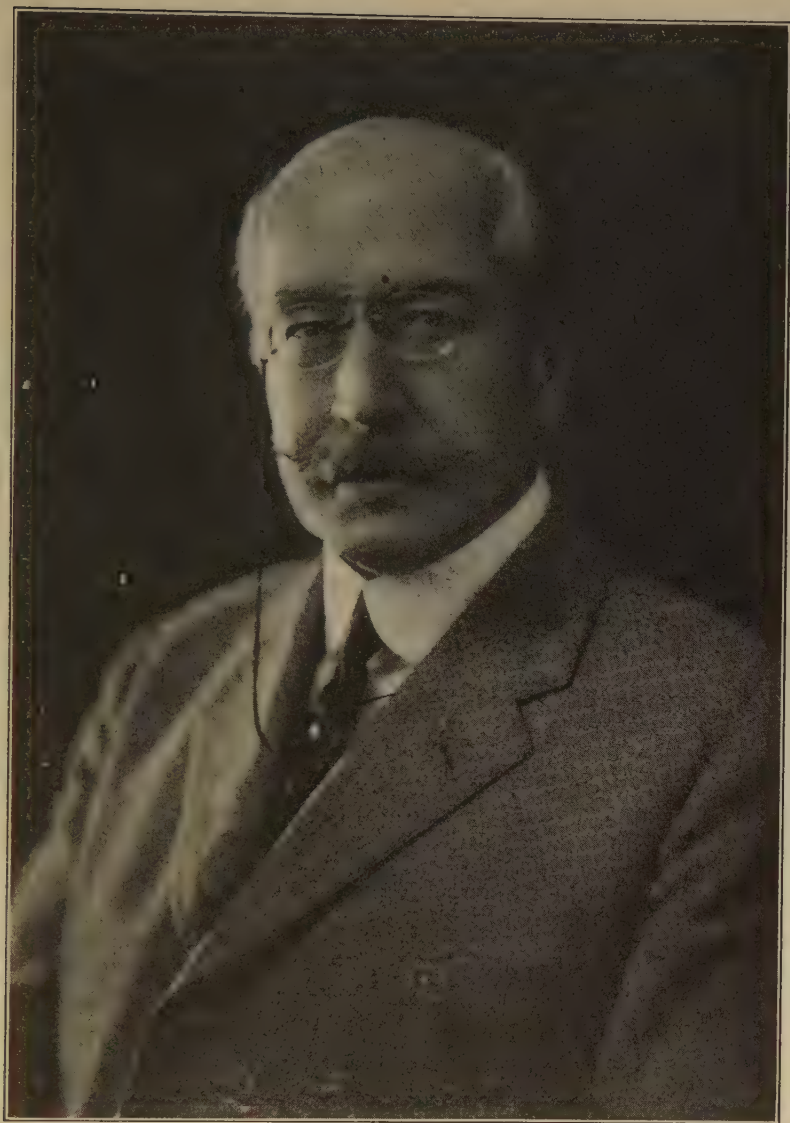


In the case of one of the isomers of inositol, moreover, we find a pair of enantiomorphs corresponding to a pair of asymmetric structures with no one asymmetric carbon atom:



QUESTIONS

1. Define and illustrate (a) carbocyclic compound; (b) heterocyclic compound; (c) cycloparaffin; (d) alicyclic compound.
2. Write equations for the reactions of olefins and cycloparaffins with bromine, dilute aqueous KMnO_4 , and ozone.
3. Write equations for the following reactions:
 - (a) Cyclopentanol + $\text{K}_2\text{Cr}_2\text{O}_7 + \text{H}_2\text{SO}_4 \rightarrow$
 - (b) Cyclohexanone + phenylhydrazine \rightarrow
 - (c) 1-Methylcyclohexene + bromine \rightarrow
 - (d) Cyclopropane + bromine \rightarrow



MARSTON TAYLOR BOGERT (1868-)

Professor of organic chemistry, Columbia University, has done extensive work in synthetic organic chemistry and has had much to do in building up a school of organic chemistry in America.

CHAPTER XX

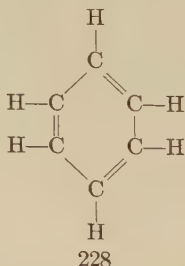
AROMATIC HYDROCARBONS

The division of carbon compounds into "aliphatic" and "aromatic" is no less arbitrary than the division of chemistry into "organic" and "inorganic." The word "aromatic" came into use because many naturally occurring substances had an agreeable aroma (such as oil of bitter almonds, oil of wintergreen, vanillin, gum benzoin, and turpentine oil), and they were put into a class by themselves. But a classification based on odor is of little value. Many of the aliphatic compounds (such as the esters) have an agreeable odor, and many belonging to the aromatic series possess little or no odor.

Aliphatic compounds (the compounds so far considered) have been represented as open-chain compounds; the aromatic compounds will be represented by closed-chain or ring formulas.

The aromatic compounds as a whole play a less important part in the chemical composition of living matter than the aliphatic series. The proteins, fats, carbohydrates, and phosphatides are largely of the aliphatic variety. On the other hand, many of the medicinals (drugs, antiseptics, etc.) belong in the aromatic series. From the industrial standpoint, the vast group of synthetic dyes is largely recruited from the aromatic series.

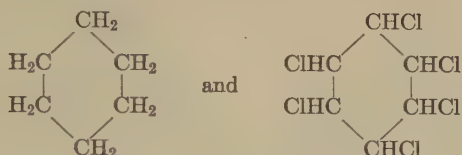
As we have seen, the mother substance of the aliphatic series is methane, CH_4 ; that of the aromatic series is benzene, C_6H_6 . It will at once be observed that, compared with methane, benzene is low in hydrogen; its structure ought, therefore, to show double or triple bonds. Its properties, however, are more those of a saturated hydrocarbon, and any structure similar in type to the one selected for ethylene or acetylene would grossly misrepresent the facts. This led *Kekulé* as far back as 1865 to propose a ring structure for benzene:



and this formula is the one generally accepted today. It is no exaggeration to say that this benzene conception of *Kekulé's* has proved of the utmost importance to the organic chemist in giving him a tool with which to devise various possible chemical reactions.

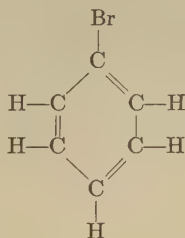
The structure of benzene, as suggested by *Kekulé*, is essentially that of a hexagon, containing six carbon and six hydrogen atoms. Any one hydrogen attached to a carbon atom is of equal importance to any other hydrogen attached to another carbon atom, and all the carbon and hydrogen atoms bear the same relationship to the molecule as a whole. There are, then, no preferences; any one atom in the molecule has exactly the same value as any other atom of the same element. The alternate double and single bonds satisfy the tetravalency of the carbon atom.

Kekulé's conception of the structure of the benzene molecule helps to explain many of the properties of benzene. According to this structure, the maximum number of hydrogen or chlorine atoms which can be added to benzene is six, giving:

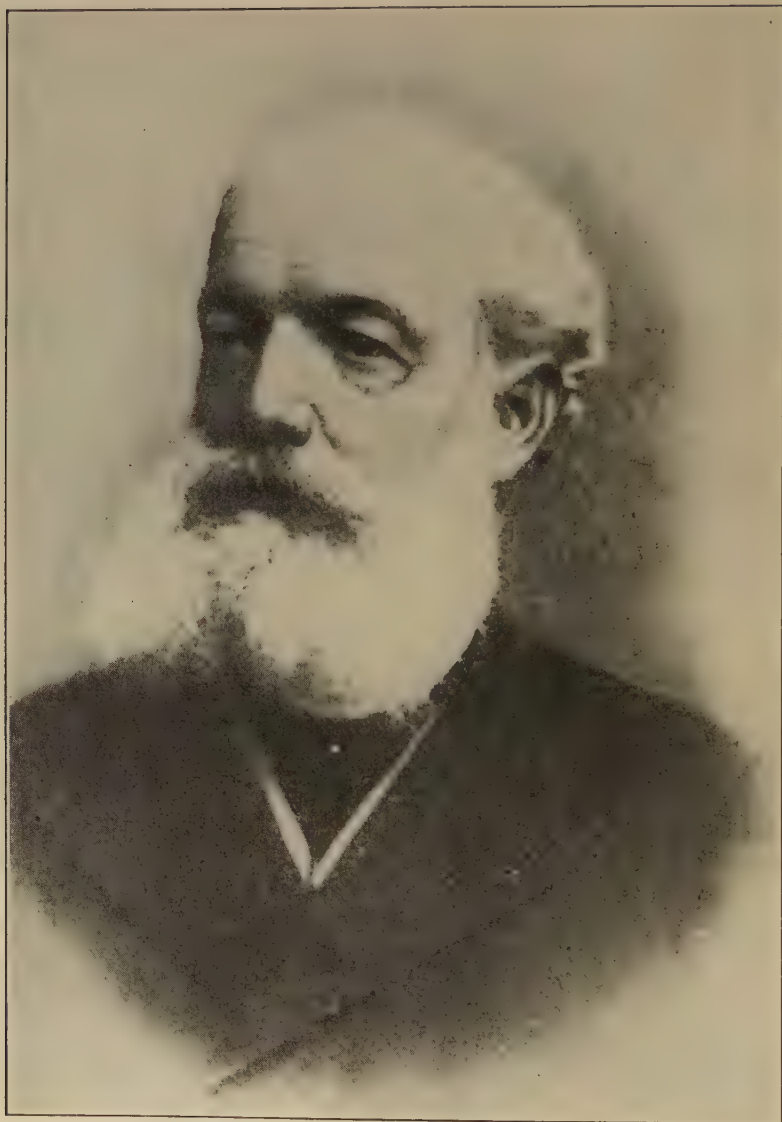


The addition of six hydrogen or six chlorine atoms implies the presence of three double bonds in the molecule.

If the benzene molecule is symmetrical and its carbon and hydrogen atoms are of equal value, then there can be one, and no more than one, monosubstitution product, and the most extensive experimental work supports this view. For example, but one monobromobenzene,



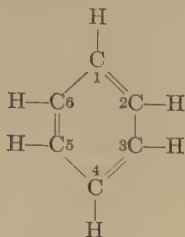
is known; it does not in the least matter to which carbon the bromine atom is attached.



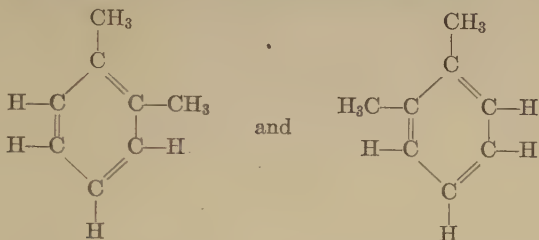
FRIEDRICH AUGUST KEKULÉ (1829–1896)

First proposed the ring structure for benzene and its compounds (p. 228).

On the other hand, *Kekulé's* benzene structure should allow for the possibility of three known isomeric disubstitution products. If we number the carbon atoms as follows:



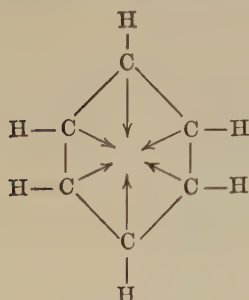
then we may have 1,2, or 1,6, or 2,3 (or any adjacent pair) of hydrogen atoms replaced, giving an *ortho* (*o*-) compound; substitution in the 1,3, or 2,6, or 3,5, or 1,5 position will give a *meta* (*m*-) compound; and substitution in the 1,4, or 2,5, or 3,6 position will yield a *para* (*p*-) compound.



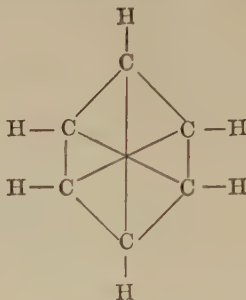
may be supposed at first sight to be different compounds, since in the one formula the methyl groups are attached to two carbon atoms having a double bond in between, whereas in the other there is no double bond. *Kekulé* made the assumption that the double and single bonds are in continuous oscillation and not static.

There were many objections in the past to representing the benzene molecule as having double bonds. The objections are still raised by every beginner in the subject. His studies of the unsaturated hydrocarbons lead him to believe that a compound whose formula has one or more double bonds is "unsaturated," and, by virtue of that fact, shows some very specific properties; but, as has already been pointed out, the properties of benzene are not really those of an unsaturated compound at all. For example, benzene, unlike the olefins, or other unsaturated aliphatic compounds, does not react with dilute potassium permanganate; it does not react with hydrogen bromide; and with bromine it forms substitution rather than addition compounds. This

has led a number of investigators to suggest formulas for benzene which do not contain the usual type of double bonds, such as:



Armstrong-Baeyer
formula



Claus formula

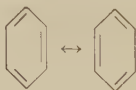


Thiele formula

Thiele's formula is simply the result of his representation of the double bond. It emphasizes the existence of a completely conjugated system of alternating single and double bonds. Such a structure would not be olefinic in nature, since it would be a much more stable system than the double bonds lead us to expect. However, *Kekulé's* formula is still preferred by the majority of organic chemists, because it explains many of the chemical characteristics of benzene and its derivatives.

From the more modern viewpoint of resonance, benzene, with its cyclic conjugation, provides a beautiful example of a resonating system (p. 56), the several representations of which differ only in the different arrangements of six electrons.

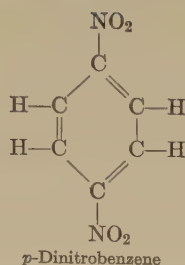
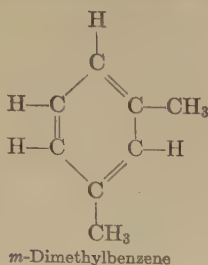
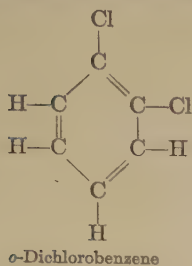
The principal resonating structures are the two *Kekulé* formulations:



The C—C distance in benzene is 1.39 Å, which is between the corresponding distance in aliphatic (1.54) and in olefinic (1.34) compounds. This corresponds to the so-called aromatic behavior of benzene and its derivatives, which is quite characteristic, as we shall see, and which is intermediate between the paraffinic behavior of single-bond aliphatics and the olefinic behavior of double-bond compounds.

Thus, the concept of resonance not only serves to explain the unusual stability and properties of the six-carbon aromatic ring, but also provides modern support for *Kekulé's* structure and his assumption of oscillation.

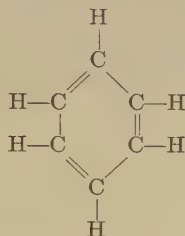
Examples of benzene disubstitution products are:



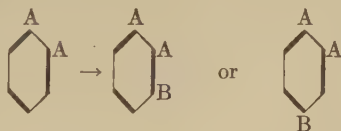
To simplify the writing of benzene and its derivatives, we shall henceforth represent its structure as:



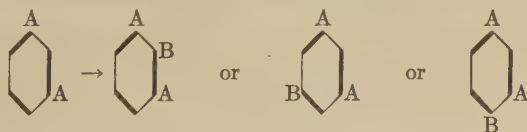
(heavy lines indicating double bonds and light lines single bonds), bearing in mind that what is really meant is:



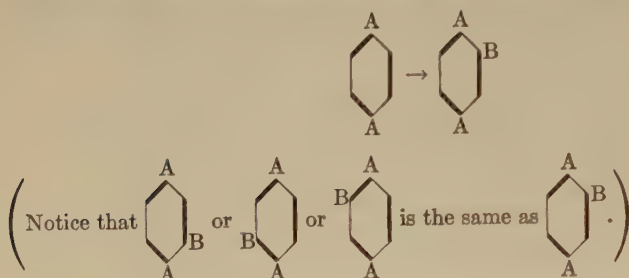
Körner's method of determining the position of groups. (*Orientation.*) Granting that three disubstitution products of benzene are possible, how can we prove that a particular one is *ortho*, another *meta*, and a third *para*? This can be done by converting the di- into tri-derivatives. For example, if the compound is *ortho*, two and only two trisubstitution products are possible:



If the compound is *meta*, three trisubstitution products are possible:

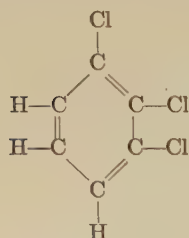


If the compound is para, but one trisubstitution product is possible.

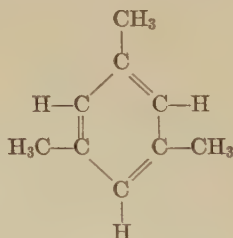


This applies only to the instance in which both initial substituents are the same (A), a case which is quite common in practice.

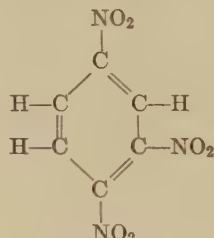
Other methods may be used to determine the relative positions of substituents in the benzene ring. For instance, it may be simple in some cases to convert the original substituent groups into others to yield compounds of known orientation. For example, a hydrocarbon which is oxidized to benzene-*ortho*-dicarboxylic acid (phthalic acid, p. 298) must be a compound in which there are two alkyl side chains in the *ortho* position. Theoretically, only three trisubstitution products are possible where the substituents are the same, and only three are actually known; i.e.,



1,2,3-Trichlorobenzene
(adjacent or vicinal)

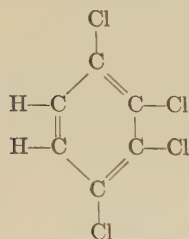


1,3,5-Trimethylbenzene
(symmetrical)

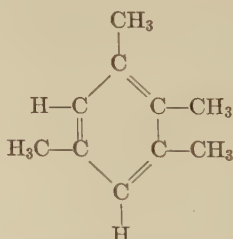


1,3,4-Trinitrobenzene
(unsymmetrical)

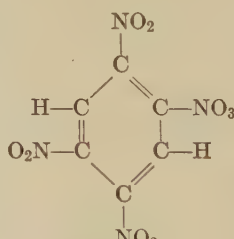
Where the tetrasubstitution products have like substituents, three isomers are possible:



1,2,3,4-Tetrachlorobenzene

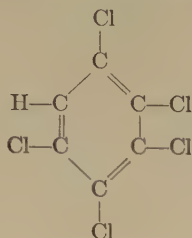


1,2,3,5-Tetramethyl-
benzene



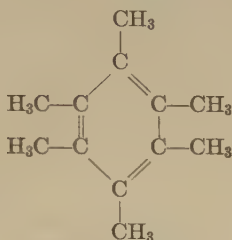
1,2,4,5-Tetranitro-
benzene

With five substituents, but one compound is possible:



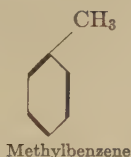
Pentachlorobenzene

With six substituents but one compound is possible:



Hexamethylbenzene

In the compounds

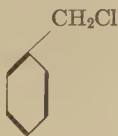


Methylbenzene



Ethylbenzene

the CH_3 and C_2H_5 groups are spoken of as "side chains," the benzene residue being the "nucleus." Substitution may take place in the side chain, or in the nucleus, or in both, yielding various products; for example:



Benzyl chloride ¹



p-Chlorotoluene



p-Chlorobenzyl chloride

Sources of Aromatic Hydrocarbons. Since *Perkin's* discovery of a dye made from products of coal-tar distillation, coal tar has become a

¹ The $\text{C}_6\text{H}_5 \cdot \text{CH}_2$ (monovalent) group is known as the "benzyl" group.

product of prime importance and is no longer a messy and useless by-product of the manufacture of coke from bituminous coal. Modern coke ovens are designed specifically to recover the gases and the tar as efficiently as possible.

The accompanying chart presents a list of the principal products obtained from the distillation of coal tar, among which we find the mother substances of the aromatic series of compounds, such as benzene, toluene, xylenes, naphthalene, and anthracene.

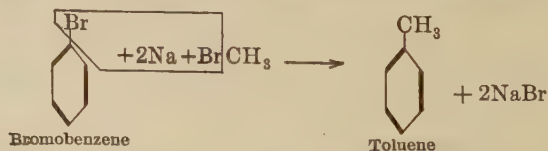
Petroleum is now also a significant source of aromatic hydrocarbons. Not only do certain petroleums yield quantities of benzene, toluene, etc., by fractionation, but some cyclic hydrocarbons are made in large quantities by the cyclization of paraffins of the same number of carbon atoms, a process called "hydroforming" (p. 30).

"Benzene" is to be sharply distinguished from "benzine." Benzine represents a mixture of hydrocarbons obtained from petroleum, whereas benzene, as we have seen, is a definite chemical compound, C_6H_6 . Benzene is also sometimes called "benzol," a word we owe to German chemists. This name has little to recommend it and, moreover, is confusing, since the ending *-ol* is usually reserved for substances containing the OH group. In the industries, the expression "90 per cent benzol" signifies the fraction which distils below $100^\circ C$; it contains about 70 per cent of benzene.

Benzene and Some of Its Homologs. Benzene is the starting point of a homologous series, C_nH_{2n-6} :

Benzene,	C_6H_6	C_6H_5 group = phenyl (monovalent)
Toluene, methylbenzene,	C_7H_8	C_7H_7 group = tolyl (monovalent)
Xylenes, dimethylbenzenes,	C_8H_{10}	C_8H_9 group = xyllyl (monovalent)
Mesitylene, <i>sym</i> -trimethylbenzene,	C_9H_{12}	The monovalent radicals of the aromatic hydrocarbons are known as the aryl radicals. (Cf. alkyl groups.)

General Methods of Preparing Aromatic Hydrocarbons. These hydrocarbons may be prepared by the *Fittig* synthesis, analogous to the *Wurtz* reaction already studied, which consists of treating a mixture of the appropriate halides with sodium in anhydrous ether; e.g.,



or by the *Friedel-Crafts* synthesis, in which the aromatic hydrocarbon and the appropriate halogen compound are made to react in the presence

COAL PRODUCTS CHART

Compiled by
Professor ALEXANDER LOWY, University of Pittsburgh

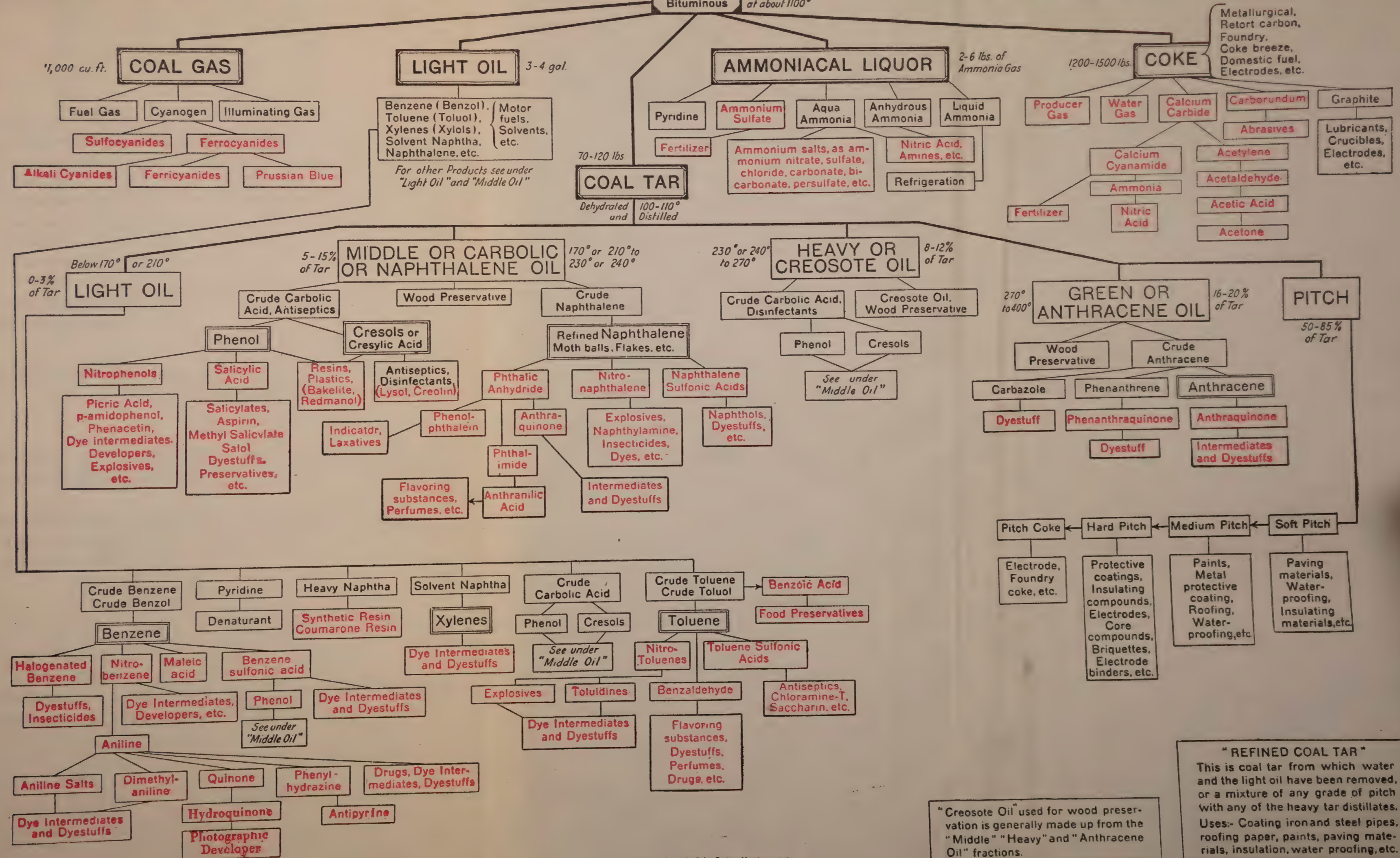
Black Type indicates Products directly obtained from Coal.

1 Ton

COAL
Bituminous

Destructive
Distillation
at about 1100°

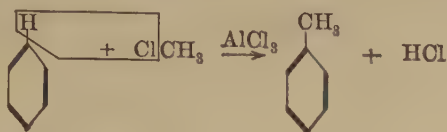
Red Type indicates Products prepared by Chemical Methods.



"Creosote Oil" used for wood preservation is generally made up from the "Middle" "Heavy" and "Anthracene Oil" fractions.

"REFINED COAL TAR"
This is coal tar from which water and the light oil have been removed, or a mixture of any grade of pitch with any of the heavy tar distillates. Uses:- Coating iron and steel pipes, roofing paper, paints, paving materials, insulation, water proofing, etc.

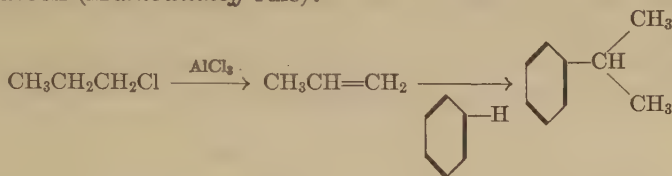
of anhydrous aluminum chloride:



In this reaction HX is eliminated; the H atom must be linked to a carbon in a ring, while the X atom must be linked to a carbon not in a ring, or, in other words, "aromatic hydrogen" and "aliphatic halogen."

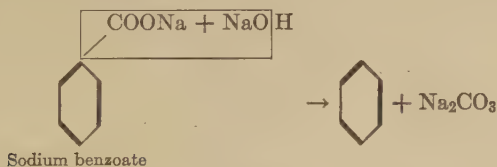
With halides higher than ethyl, normal halides undergo rearrangement in the *Friedel-Crafts* synthesis to yield mainly branched-chain alkyl benzenes and homologs; for example, *n*-propyl halides give mainly isopropyl benzene; *n*-butyl halides, secondary butyl benzene.

This is what should happen if the alkyl halides were first converted to olefins (anhydrous AlCl_3 , the catalyst, forms complexes of the type $[\text{AlCl}_4]^-$ with halide ions), which would then add to the aromatic hydrocarbon (*Markownikoff* rule):

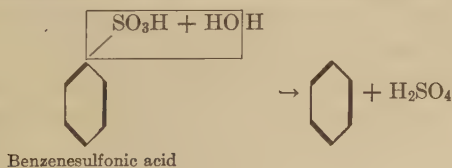


The probability of this mechanism is supported by the fact that the olefins themselves add to aromatic hydrocarbons in the *Friedel-Crafts* reaction.

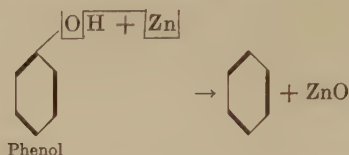
Aromatic hydrocarbons may also be prepared by heating the salts of aromatic acids with soda lime—a reaction similar to one used in the preparation of the paraffins; e.g.,



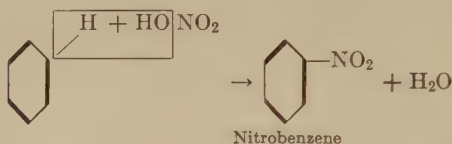
or by the elimination of the SO_3H group from benzene compounds (by the use of steam, in the presence of acids); e.g.,



or by distilling phenols with zinc dust; e.g.,

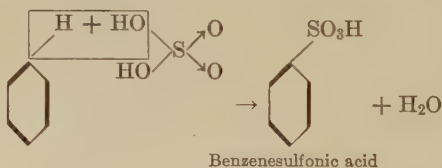


General Reactions of Aromatic Hydrocarbons. Aromatic compounds react with nitric acid (in the presence of concentrated H_2SO_4), forming nitro derivatives; e.g.,



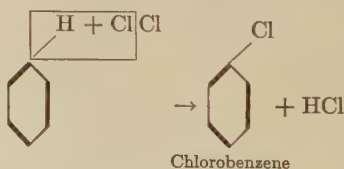
This is known as **nitration** and is generally carried out with a mixture of concentrated nitric and sulfuric acids. The sulfuric acid acts as a dehydrating agent.

These hydrocarbons also react with concentrated sulfuric acid to form sulfonic acids, usually at higher temperatures, e.g.,



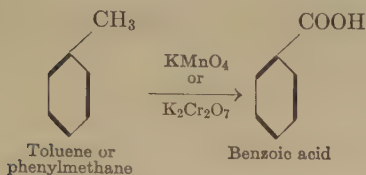
This is known as **sulfonation**.

Halogenation (Cl_2 , Br_2) forms substitution products in the presence of iron, aluminum, or iodine (catalysts or "carriers") in the cold; for example,



As we have just seen, the hydrogen of aromatic hydrocarbons can be replaced by alkyl groups by means of the *Friedel-Crafts* reaction, which is a method of **alkylation**. This term now includes also a variety of reactions in which alkyl groups are attached to aliphatic hydrocarbons.

The "side chain," whether CH_3 or any other alkyl group, may be oxidized to the carboxyl group, COOH ; e.g.,

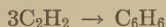


The four principal reactions of benzene hydrocarbons—nitration, sulfonation, halogenation, and alkylation—typify “aromatic” behavior, which, incidentally, is manifested by other types of cyclic structures (naphthalene, anthracene, furan, etc.). These reactions are substitutions, a distinction from unsaturated aliphatic hydrocarbons. In addition, the substitution of aromatic hydrocarbons proceeds to give satisfactory yields and can be controlled—an essential difference from substitution in paraffins.

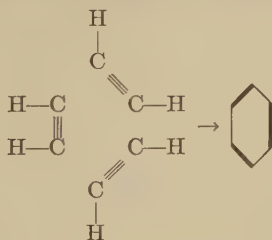
AROMATIC HYDROCARBONS

Benzene, C_6H_6 , is the mother substance of the aromatic hydrocarbons. Commercially, it is obtained from the fractional distillation of coal tar. It is also present in California petroleum. It is a colorless liquid (b.p. 80.4°), burning with a smoky flame (owing to the high percentage of carbon), and when its vapor is mixed with air and ignited it is explosive. It is used as a solvent for fats, resins, etc., and in the manufacture of a large number of aromatic compounds; e.g., nitrobenzene and chlorobenzene. Crude benzene (benzol) is used extensively in motor fuel. Benzene is a narcotic which when swallowed or inhaled produces vertigo, delirium, and convulsions.

Even though the syntheses of benzene are of no practical value, they possess some academic interest for the light they throw on the structure of the compound and on the relations between aromatic and aliphatic nuclei. One historical method is to pass acetylene through a red-hot tube:

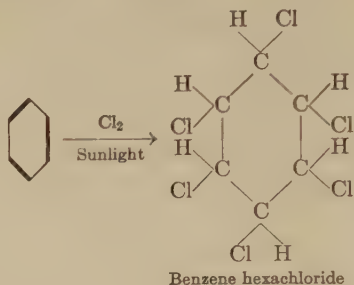


Here we have an example of passing from an aliphatic to an aromatic compound—in this particular method, by polymerization:



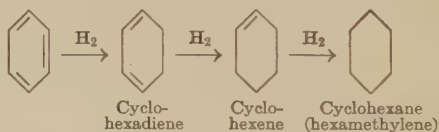
The cyclization of *n*-hexane to benzene provides another example.

In contrast to the ease of substitution is the slow and difficult addition of chlorine and hydrogen to benzene:



Hydrogen addition (in the presence of catalysts), which is an exothermic reaction for olefins, is endothermic for the first mole of hydrogen in the case of benzene.¹ This emphasizes once more the extraordinary stability of the benzene nucleus.

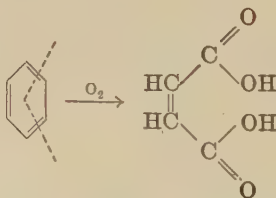
Further hydrogenation proceeds more easily, since we are now dealing with an alicyclic, not an aromatic, structure:



These hydroaromatic hydrocarbons are known as alicyclics or naphthenes (Chapter XIX).


In the vapor phase, benzene can be hydrogenated directly in the presence of nickel (*Sabatier* and *Senderens*).

Air oxidation of benzene over vanadium pentoxide is the commercial method of making maleic acid:



Here is an example of the formation of an aliphatic structure from an aromatic one, and it requires rather drastic and special conditions.

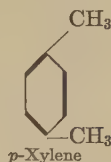
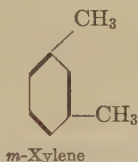
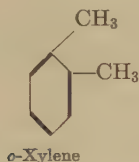
¹ The excess energy required to hydrogenate the first double bond of benzene is known as the *resonance energy* of the compound.

Toluene, , or phenylmethane, or methylbenzene (b.p. 111°),

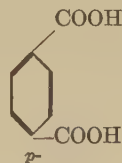
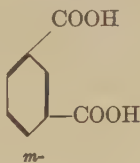
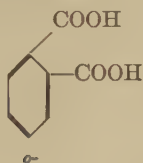
is obtained from the fractional distillation of coal tar and also, in even larger quantities now, by the cyclization of *n*-heptane from petroleum ("hydroforming"). Toluene was obtained originally by the distillation of balsam of Peru and Tolu; it can also be prepared by a *Friedel-Crafts* synthesis. Its properties are, of course, similar to those of benzene. When oxidized it yields benzoic acid (p. 294).¹


Toluene is a vital or "critical" material in war time, because TNT, trinitrotoluene (p. 259), is undoubtedly the principal explosive in modern warfare. Toluene is also used extensively as a solvent in the rubber, lacquer, and munition industries. It is poisonous when inhaled.

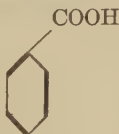
Xylenes, or dimethylbenzenes. Since these are disubstitution products, three isomers are known:



They are obtained from coal tar. On oxidation, the xylenes give the corresponding dibasic acids, phthalic acids:

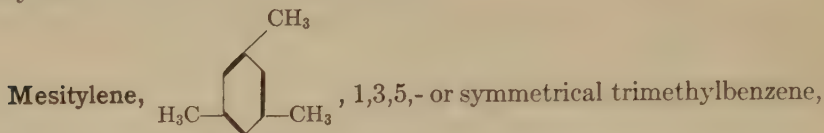


Ethylbenzene, , is an isomer of the xylenes but is easily distinguished from them by the fact that on oxidation it yields benzoic acid,

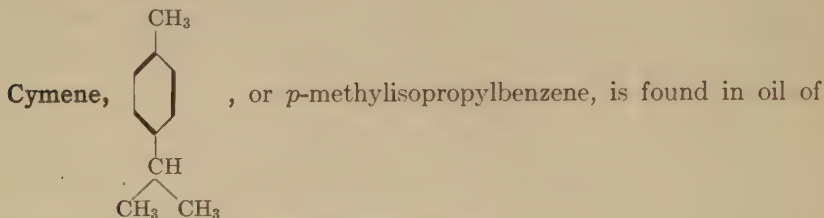


¹ C₆H₅, monovalent, is known as the phenyl group.

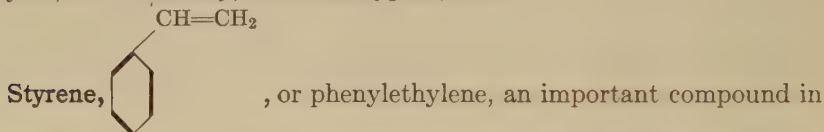
It is made by a *Friedel-Crafts* reaction with ethyl chloride or with ethylene.



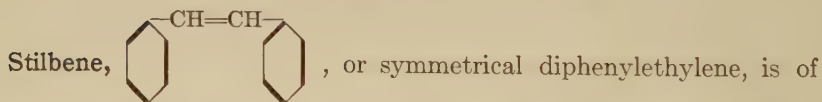
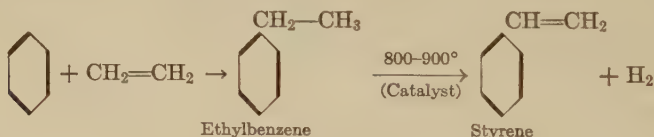
is found in coal tar.



thyme, oil of caraway, oil of eucalyptus, etc.

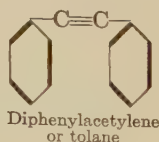
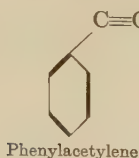


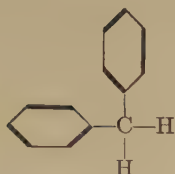
the manufacture of resins and synthetic rubber, is prepared by reacting ethylene and benzene in the vapor phase at 200–300° C and then dehydrogenating the ethylbenzene so formed:



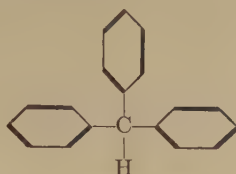
interest because a derivative, stilbestrol, exhibits the properties of a female hormone (p. 401).

The number of hydrocarbons containing the benzene nucleus is large. Some are derived from coal tar; others are synthesized. A few more of these compounds will be mentioned:

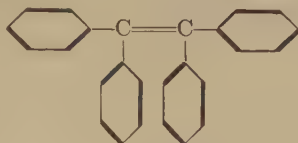




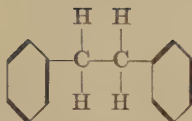
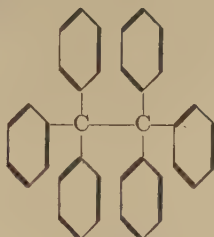
Diphenylmethane



Triphenylmethane



Tetraphenylethylene

Symmetrical
diphenylethane

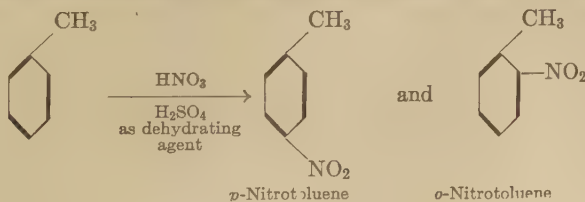
Hexaphenylethane

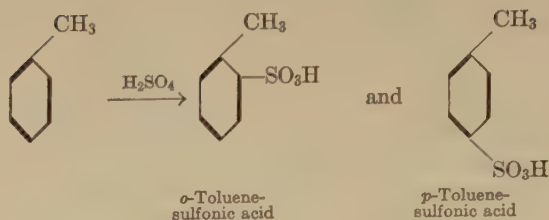
Substitution and Orientation in the Benzene Ring. *If any one of the elements or groups F, Cl, Br, I, R, OH, OR, CH₂X, NH₂, NHR, NR₂, —NH·COR, —CH₂COOH, O·COR, SH, SR, or C₆H₅ is present in the ring, an element or group that may next be introduced will take mainly the p and o positions with respect to the first group.*

2. *If any one of the groups NO₂, SO₃H, CHO, COOH, COOR, CO·R, SO₂Cl, SO₂NH₂, CCl₃, NH₃X, or CN is in the ring, an element or group that may next be introduced will take mainly the m position with respect to the first group. (The amounts of m, p, and o products formed depend very largely upon such factors as temperature, concentration of reacting substances, the type of dehydrating agent, and other experimental factors.)*

It is essential before the student proceeds any further with the text that he master thoroughly these rules and their applications.

An example of the application of these rules is immediately seen in toluene. Toluene contains a methyl (R) group; hence, a second group will proceed simultaneously to the p- and o-positions; for example,





At low temperatures, the *o*- predominates; at high temperatures, the *p*-.

When two substituents are already in the benzene ring, their orienting influences may reinforce or oppose each other. If they oppose, some further generalizations may be made:

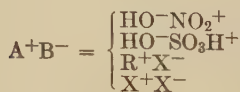
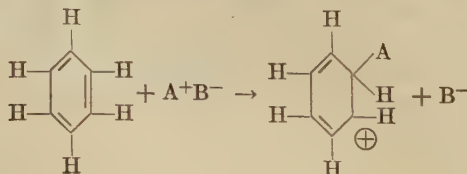
(a) Any *o*- or *p*-directing group takes precedence over any *m*-directing group.

(b) *o*- and *p*-directing groups facilitate, *m*-directing groups retard, substitution.

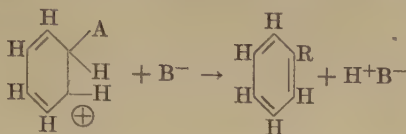
The reactivity of aromatic hydrocarbons and the importance of their numerous derivatives account for the large amount of theoretical speculation concerning reaction and orientation in the benzene ring. Many empirical rules have been enunciated to describe in general terms the orienting effect of substituent groups. The value of such rules is doubtful, since it is probably easier to learn which groups direct *o*- and *p*- and which *m*-.

Modern applications of the electron theory, however, provide a more fundamental view of the problem in terms of molecular structure (*Ingold, Robinson, Lucas, Price*). Although it is beyond the scope of this book to discuss such matters in detail, a rather rough summary of some of the outstanding theories may be of interest.

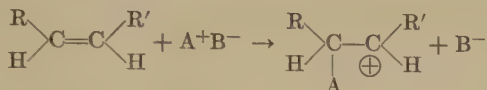
The important aromatic substituents are positive ("cationoid," "electrophilic") groups: NO_2^+ , SO_3H^+ , R^+ (alkyl), X^+ ($\text{X}_2 \rightarrow \text{X}^+ + \text{X}^-$; X^- forms HX). The initial step of the substitution may be an addition which creates an electron deficiency in the molecule; for example,



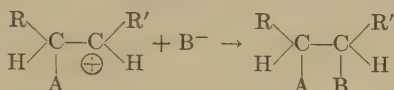
This structure can be stabilized by the loss of a proton:



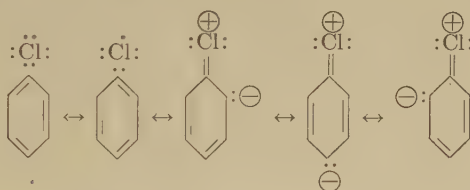
A similar mechanism may well picture the situation of the olefinic double bond:



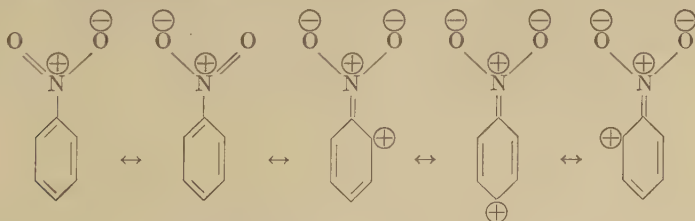
In this case, however, the intermediate complex is stabilized by the addition of the negative ("anionoid," "nucleophilic") addendum:



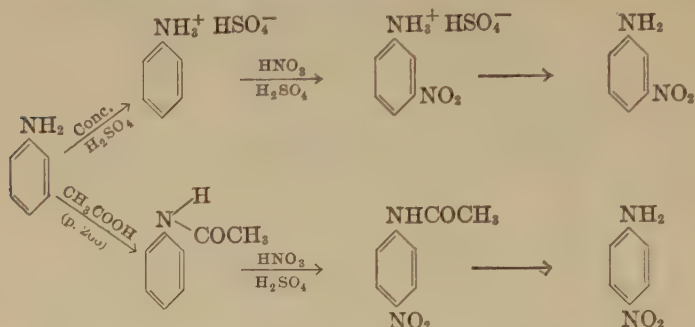
From this point of view, substituent groups already present in the benzene nucleus influence the electronic distribution in such a way that either the *o*- and *p*- or the *m*-positions are relatively more negative (owing to greater "electron density") than the other positions. This can occur through the existence of resonating forms (p. 56); for example,



The *o*- or *p*-directing groups are those which lose electrons *to* the ring, or which carry unshared pairs of electrons which can establish conjugation with the ring. The *m*-directing groups, on the other hand, are those in which a dipole exists, the positive atom being attached to the ring, and thus attracting electrons *from* the ring:



The effect of the polarity of the orienting group is shown in the nitration of aniline under different conditions:

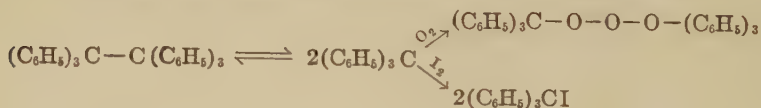


FREE RADICALS

In the attempt to prepare hexaphenylethane *Gomberg* allowed silver, zinc, and mercury to react with triphenylchloromethane (compare *Wurtz* reaction, p. 19):



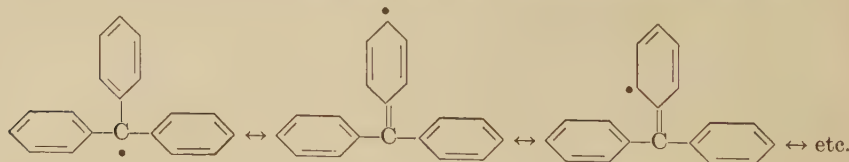
The compound formed was colorless in the solid state but yellow in solution. The colored solution readily absorbed oxygen from the air, to form a colorless product which when isolated was shown to be a peroxide, $(\text{C}_6\text{H}_5)_3\text{C}-\text{O}-\text{O}-\text{C}(\text{C}_6\text{H}_5)_3$. These and other facts (such as the absorption of iodine from benzene solutions) led to the view that in solution hexaphenylethane dissociates into triphenylmethyl:



In fact, in solution, triphenylmethyl is an equilibrium mixture of the monomer and the dimer, with very little of the monomer.

This triphenylmethyl is an example of a *free radical*, with carbon having a "valence" of three. It is a neutral group with an odd electron.

From the structural point of view, the unusual stability of such radicals may be explained by the possible existence of comparatively large numbers of resonating forms. For instance, whereas C_6H_5 has three contributing structures, there are ten for triphenylmethyl, such as



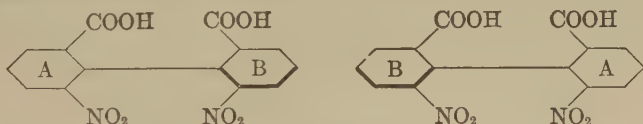
In the case of $(\text{C}_6\text{H}_5)_3\text{C}$, we can write nineteen resonating forms. This is in accord with the fact that more complex structures, such as the last one, exist dissociated in larger amounts than the simpler free radicals. On the same basis, those aliphatic free radicals which have been detected should be very unstable. Actually they have been found to be extremely short-lived.

The proof of the existence of free methyl radicals we owe to *Paneih*, among others. He showed that lead tetramethyl, $\text{Pb}(\text{CH}_3)_4$, heated at low pressures and in the presence of hydrogen, is decomposed into lead and free methyl. The free methyl groups are made to combine with metallic mirrors (such as Pb, Sb, Zn, or Cd) formed on the walls of the vessels. The metallic derivative distills off. This disappearance indicates the existence of the free radical. The half life of these free methyl groups was found to be 0.006 second. The free ethyl radical has also been prepared, and its properties are similar to those of the methyl radical. Such free radicals are intermediates, assumed or proven, in many reaction mechanisms.

Diphenyl, biphenyl, xenene, , or phenylbenzene, is made by

the dehydrogenation of two moles of benzene at an elevated temperature. Its high boiling point and its stability render this compound a very useful substitute for steam in boilers; it enables the boiler to run at a higher temperature. Diphenyl, like benzene, may be chlorinated, nitrated, sulfonated, etc.

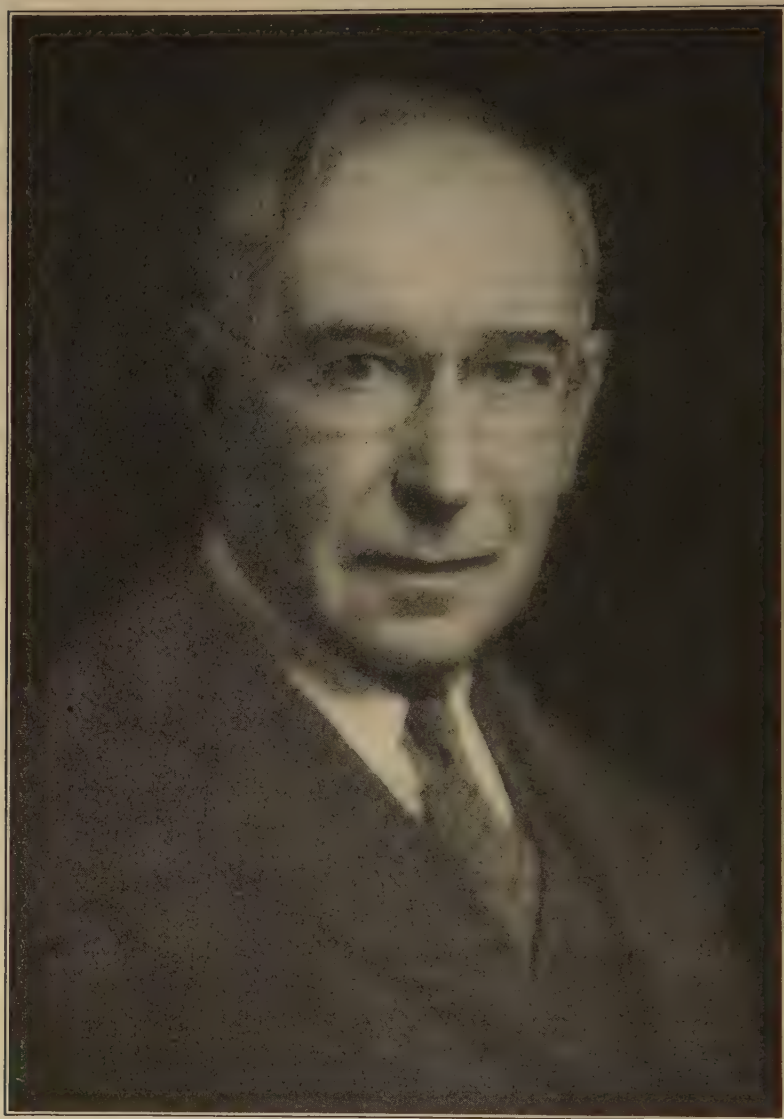
Some 2,2',6-trisubstituted and 2,2',6,6'-tetrasubstituted diphenyls have been resolved into optically active isomers (*Roger Adams*); e.g.,



Here we have an asymmetric molecule without an asymmetric atom (p. 146); the two structures are not superposable because free rotation about the connecting bond is prevented by the size of the substituent groups (*steric hindrance*). Smaller substituents such as F and CH_3 do not impede this rotation, and no enantiomorphs have been isolated in such cases.



¹ Ring A is in the plane of the paper, and ring B is in a plane perpendicular to ring A.



MOSES GOMBERG (1866-)

Professor of chemistry at the University of Michigan, one of the pioneer workers on trivalent carbon and free radicals (p. 246).



ROGER ADAMS (1889-)

Professor and head of the department of chemistry, University of Illinois. He is one of the outstanding organic chemists in America and has contributed to our knowledge of the chemistry of chaulmoogric acid (used in the treatment of leprosy), of the stereochemistry of the diphenyl series, etc. He has been awarded the Nichols and the Willard Gibbs medals.

The last three compounds mentioned belong to the "conjugated" or condensed cyclic series and will be taken up in detail in Chapter XXVII.

QUESTIONS

1. What reactions chiefly differentiate the aromatic hydrocarbons from the aliphatic hydrocarbons? Write the equations, and name the compounds.
2. Write equations for several different methods of preparing aromatic hydrocarbons.
3. Differentiate clearly between (a) aliphatics; (b) aromatics; and (c) alicyclics.
4. Distinguish between (a) benzene; (b) benzine; (c) 90 per cent benzol; (d) benzol.
5. Write structural formulas for the following compounds: (a) cyclopropane; (b) heptamethylene; (c) toluene; (d) *o*-xylene; (e) *m*-xylene; (f) triphenylmethane; (g) *p*-xylene; (h) phenyl chloride; (i) mesitylene; (j) cymene; (k) bromobenzene; (l) hexachlorobenzene; (m) hexahydrobenzene; (n) benzenesulfonic acid; (o) nitrobenzene; (p) phenylethylene; (q) triphenylmethyl; (r) hexamethylbenzene; (s) hexachlorohexahydrobenzene; (t) *p*-bromotoluene; (u) isopropylbenzene; (v) diphenyl; (w) inositol; (x) tetrahydrobenzene; (y) cyclobutane; (z) styrene; (aa) 4-chlorotoluene; (ab) 2,2'-dichlorodiphenyl.
6. Describe the following syntheses: (a) *p*-dibromobenzene from benzene; (b) *p*-nitrobenzoic acid from benzene and methanol.
7. Write equations for the following reactions:
 - (a) *p*-Bromotoluene + isopropyl bromide + sodium \rightarrow
 - (b) Chlorobenzene + ethyl chloride + anhydrous $\text{AlCl}_3 \rightarrow$
 - (c) Ethylbenzene + HNO_3 (+ H_2SO_4) \rightarrow
 - (d) Toluene + $\text{H}_2\text{SO}_4 \rightarrow$
 - (e) *n*-Butylbenzene + $\text{KMnO}_4 \rightarrow$
 - (f) Benzene + H_2 (+ catalyst) \rightarrow
 - (g) Triphenylchloromethane + zinc \rightarrow
 - (h) Diphenyl + HNO_3 (+ H_2SO_4) \rightarrow

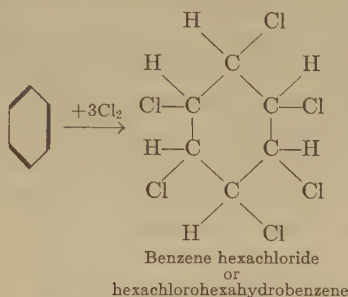
CHAPTER XXI

HALOGEN DERIVATIVES, SULFONIC ACIDS, AND NITRO DERIVATIVES OF THE AROMATIC HYDROCARBONS

HALOGEN COMPOUNDS ¹

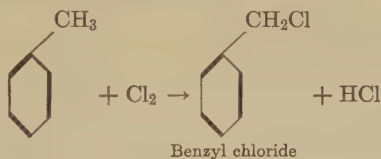
The halogens may react in one of three ways with aromatic hydrocarbons:

1. They may form addition products; e.g.,



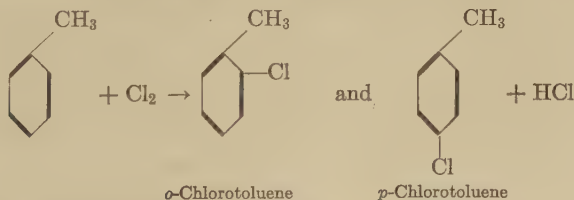
This process needs exposure to sunlight, but no carrier or catalyst. It is a slow reaction.

2. They may substitute in the side chain; e.g.,



This reaction is accomplished at the boiling temperature of toluene, in the presence of sunlight, or artificial light containing ultraviolet rays, but in the absence of a catalyst or halogen carrier.

3. The halogen may substitute in the ring; e.g.,



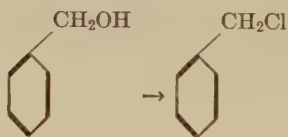
This process needs ordinary temperature, no sunlight, and a carrier.

¹ At this point the student is advised to review the chapter on aliphatic halogen compounds, p. 49.

The usual halogen "carriers," or catalysts, are FeCl_3 , FeBr_3 , AlBr_3 , Fe , P , S , I , etc. These substances are capable of forming complexes with Cl^- (for example, FeCl_4^-), so that substitution may be assumed to proceed with Cl^+ .


Preparation. The halogen derivatives of the aromatic series may be prepared by direct halogenation with Cl_2 or Br_2 , as just described (iodine does not react unless an oxidizing agent, such as mercuric oxide or concentrated HNO_3 , is present to react with the liberated HI), or by the conversion of the corresponding amino compound into the halogen derivative, where the halogen takes the place of NH_2 ; this is done by means of the diazo reaction (p. 269).

Ethyl alcohol can be treated with hydrogen bromide, in the presence of sulfuric acid, to give $\text{C}_2\text{H}_5\text{Br}$, but, when phenol, $\text{C}_6\text{H}_5\text{OH}$, is treated with hydrogen bromide, no analogous reaction takes place. Again, when ethyl alcohol is acted on by phosphorus pentachloride, PCl_5 , we get $\text{C}_2\text{H}_5\text{Cl}$; but when phenol is similarly treated, only a small yield of chlorobenzene, $\text{C}_6\text{H}_5\text{Cl}$, is obtained. On the other hand, benzyl alcohol is readily transformed into benzyl chloride by PCl_5 :



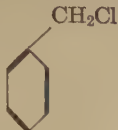
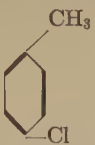
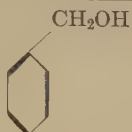
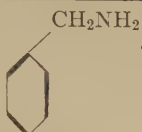
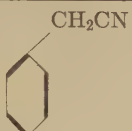
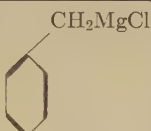
Notice that here the side chain reacts. The side chain, in fact, behaves like an aliphatic rather than like an aromatic group.

In the place of chlorine the following substances are sometimes used to introduce the element: chlorosulfonic acid, ClSO_3H ; sulfuryl chloride, SO_2Cl_2 ; and sulfur mono- and dichloride, SCl and SCl_2 .

Properties. Where the X is attached to the ring as in , we get

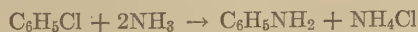
substances which may be colorless liquids or solids, with an agreeable odor, and which are stable; where the X is attached to the side chain, as in $\text{C}_6\text{H}_5\text{CH}_2\text{Cl}$, the compounds have strong, disagreeable, pungent odors, are very reactive, and act as lachrymators. In general, they show the properties of the aliphatic halogen compounds of the type RX .

Some of the properties of the two types of halogen compounds may be summarized thus:

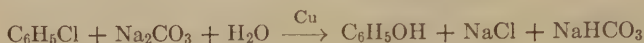
Reagents	 Benzyl chloride	 <i>p</i> -Chlorotoluene
KOH	 Benzyl alcohol	No reaction under similar conditions unless at least one NO ₂ group is <i>o</i> - or <i>p</i> - to the halogen
NH ₃	 Benzylamine	No reaction under similar conditions (see below)
KCN	 Benzyl cyanide	No reaction under similar conditions
Mg	 	No reaction with Cl; formation of Grignard reagent with Br and I

from which it may be seen that, where the halogen is attached to the nucleus, we get a relatively inactive compound; but where it is attached to the side chain, a very active compound, similar in its properties to the aliphatic halogen derivatives, is obtained. (The *Fittig* reaction exemplifies a typical reaction for the type where the halogen is attached to the nucleus.) The above reactions hold good only when carried out under atmospheric pressure. It has been found that at higher pressures reactions may be obtained even when the halogen is connected to the nucleus.

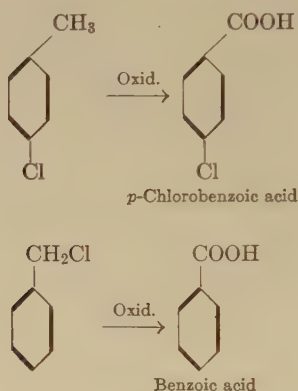
Under pressure, chlorobenzene will react with ammonia to form aniline and ammonium chloride:



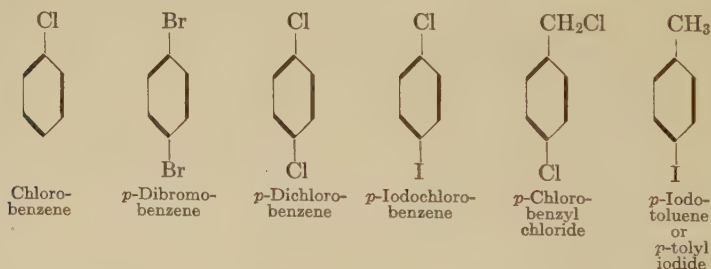
and is transformed into phenol when heated under high pressure with aqueous sodium carbonate in the presence of copper:



Whether the X is attached to the ring or to the side chain may be determined in some such way as the following:



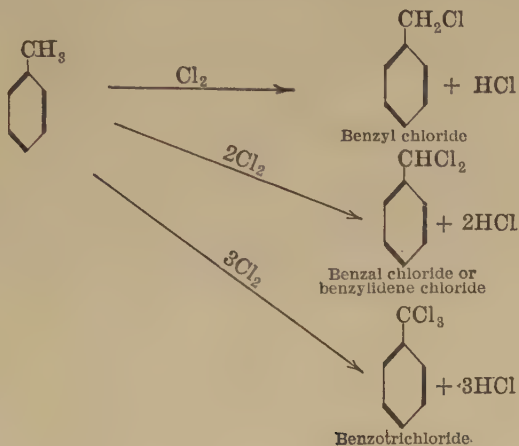
Hundreds of halogen compounds are known; only a few will be mentioned:



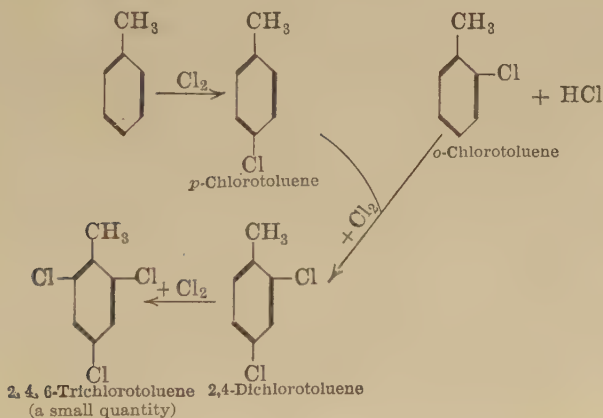
Chlorobenzene is manufactured by chlorinating benzene in the presence of iron. It is used for the manufacture of phenol (p. 278), aniline (p. 264), and other dye intermediates. *p*-Dichlorobenzene is used extensively to protect woolen goods from moths and to protect peach trees from the peach-tree borer.

We may again refer to the preparation of these halogen compounds. Toluene, when acted upon by chlorine, in the presence of sunlight or ultraviolet light, in the absence of a "carrier," in the absence of moisture,

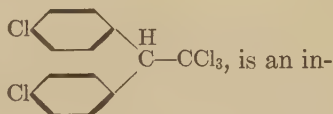
and at boiling temperature, gives the following products:



When, however, the chlorine and the toluene are made to react in the absence of sunlight and at room temperature, but in the presence of a carrier, they yield:



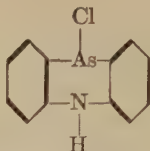
Dichlorodiphenyltrichloroethane, DDT,



secticide used effectively in World War II.

Chemical Warfare Agents. Some of the most important chemical warfare agents of World War II are aromatic halides: chloroacetophenone (official military symbol CN), $\text{C}_6\text{H}_5\text{COCH}_2\text{Cl}$, a lachrymator; diphenyl-

chloroarsine (DA), $(\text{C}_6\text{H}_5)_2\text{AsCl}$; and diphenylaminechloroarsine or Adamsite (DM),



both irritant smokes. Bromobenzyl cyanide, $\text{BrC}_6\text{H}_4\text{CH}_2\text{CN}$ (CA), is another lachrymator. Among many other compounds which have been used or suggested for similar purposes are: benzyl bromide, $\text{C}_6\text{H}_5\text{CH}_2\text{Br}$; xylol bromide, $o\text{-CH}_3\text{C}_6\text{H}_4\text{CH}_2\text{Br}$; and phenylcarbylamine chloride, $\text{C}_6\text{H}_5\text{NCCl}_2$.

Since we are on the subject of chemical warfare agents, we may include here a list of the current aliphatic "war gases." All these gases contain halogen (as do the inorganic agents, too): phosgene (CG), COCl_2 (p. 133), and chloropicrin (PS), CCl_3NO_2 , lung irritants; this class includes also Cl_2 , diphosgene (DP), and trichloromethyl chloroformate, $\text{ClC}-\text{OCCl}_3$.



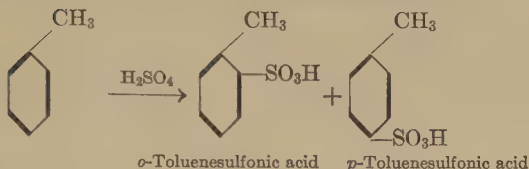
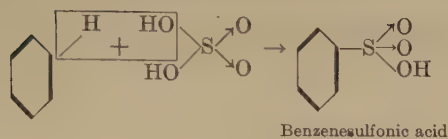
The most dangerous substances are the vesicants, which attack any part of the body and are slow and insidious in their effect: mustard gas (HS), β, β' -dichlorodiethyl sulfide, $(\text{C}_2\text{H}_4\text{Cl})_2\text{S}$ (p. 215); Lewisite (M-1), β -chlorovinylchloroarsine, $\text{ClCH}=\text{CHAsCl}_2$ (p. 218); ethyldichloroarsine (ED), $\text{C}_2\text{H}_5\text{AsCl}_2$.

Other compounds previously used or suggested are: bromoacetone, $\text{CH}_2\text{BrCOCH}_3$; chloroacetone, $\text{CH}_2\text{ClCOCH}_3$; bromoethyl methyl ketone, $\text{CH}_3\text{COCHBrCH}_3$; dichlorodimethyl ether, $(\text{CH}_2\text{Cl})_2\text{O}$; hydrocyanic acid, HCN ; cyanogen bromide, CNBr .

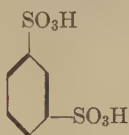
It may not be amiss to include here those inorganic substances which are used to produce screening smokes in chemical warfare: titanium tetrachloride (FM); white phosphorus (WP); HC mixture ($\text{Zn} + \text{C}_2\text{Cl}_6$); SO_3 in chlorosulfonic acid, ClSO_3H (FS).

SULFONIC ACIDS

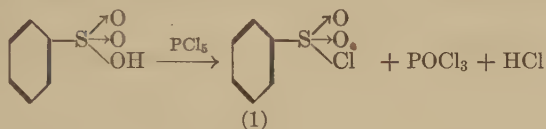
Sulfonic acids are a very important class of organic compounds since from them phenolic compounds (p. 277), naphthols (p. 324), etc., are prepared. They are generally made by the direct sulfonation of the hydrocarbon. For sulfonation, concentrated H_2SO_4 at elevated temperatures is required. Very often it is necessary to resort to fuming H_2SO_4 .



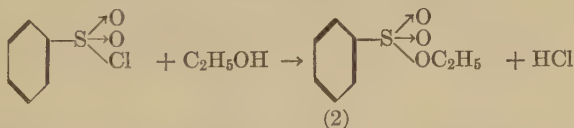
Benzenesulfonic acid when further sulfonated gives *m*-benzenedisulfonic acid:



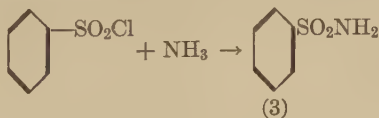
Properties. With PCl_5 the sulfonic acid gives benzenesulfonyl chloride (1):



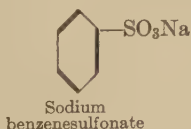
Sulfonyl chlorides can be made by the direct substitution of aromatic H with chlorosulfonic acid, a very reactive substance. (1) reacts with ethyl alcohol to give ethyl benzenesulfonate (2), an ester:



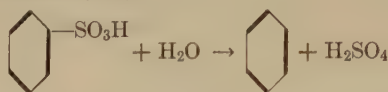
(1) also reacts with ammonia to yield benzenesulfonamide (3):



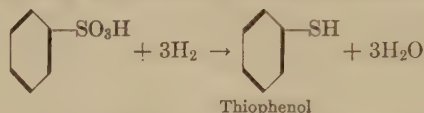
and with NaOH to form the sodium salt; e.g.,



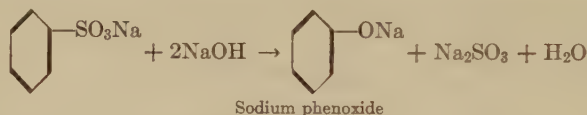
(Notice the analogous reactions of the COOH group and the SO_3H group.) With steam under pressure sulfonic acids are decomposed, yielding the hydrocarbons; e.g.,



and with hydrogen they are reduced to thiophenols; e.g.,



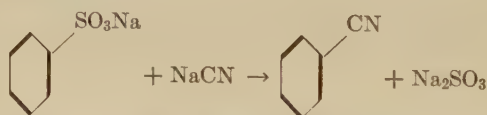
When fused with NaOH , the sulfonic acids yield the sodium salts of the phenols; e.g.,



from which the phenol, $\text{C}_6\text{H}_5\text{OH}$, can be obtained by treating the solution with CO_2 (H_2CO_3). (Carbonic acid is a stronger acid than phenol.)

This is an extremely important commercial method for the preparation of phenol and phenolic compounds. The sulfonic acid is first made from the hydrocarbon, then fused with NaOH , and the resulting compound acidified.

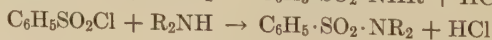
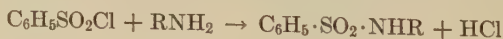
The sulfonic acids (salts) can be distilled with NaCN , yielding the corresponding cyanides; e.g.,



The free sulfonic acids are usually very soluble in water. In order to separate them from the excess of H_2SO_4 , the Pb , Ca , or Ba salts are usually prepared. The Pb , Ba , and Ca sulfonates are soluble in water whereas the sulfates are insoluble.

Quite often organic compounds insoluble in water are sulfonated, being thus converted to water-soluble sulfonic acids. This is a procedure extensively used in the dye industry.

Hinsberg Reaction for Separating and Characterizing Amines. Benzenesulfonyl chloride reacts with primary and secondary amines as follows:

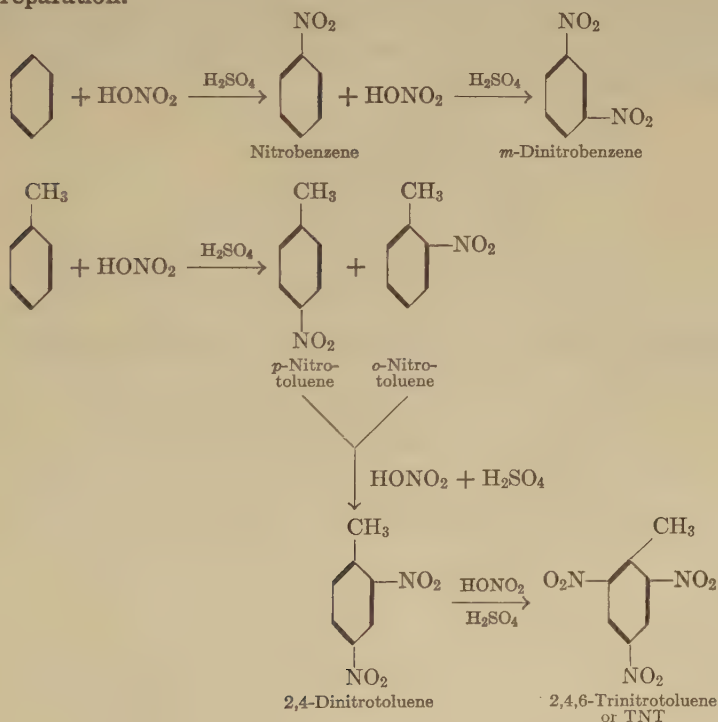


Tertiary amines do not react. The sulfonamides formed from the primary and secondary amines are treated with NaOH whereby the $C_6H_5SO_2NHR$ is converted to a *soluble* sodium salt, $C_6H_5SO_2NRNa$, the $C_6H_5SO_2NR_2$ remaining unchanged and *insoluble*.

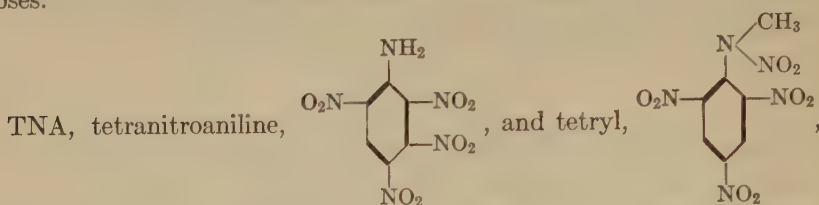
NITRO COMPOUNDS

Nitro compounds constitute a very important class of organic compounds. They are generally prepared by direct nitration with HNO_3 . In some instances the nitration proceeds readily; in others it does not. In some cases dilute nitric acid can be used (provided no oxidation takes place); in others the nitration will proceed only with concentrated or fuming nitric acid. Sometimes NO_2 is used in place of nitric acid. Usually the presence of sulfuric acid is necessary to absorb the water just as fast as it is formed in the reaction. Sometimes only fuming sulfuric acid will serve the purpose. In reality, a number of factors play their part in nitration, such as strength of nitrating acid ("mixed acid"— $HNO_3 + H_2SO_4$), amount of acid used, temperature of the reaction, length of time of nitration, and agitation of the liquids.

Preparation.

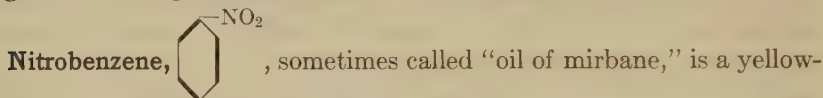


TNT, mixed with ammonium nitrate, is the principal explosive in shells and bombs. It is also used for mines and for demolition purposes.

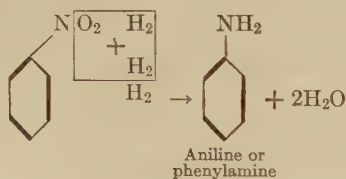


2,4,6-trinitrophenyl methyl nitroamine, are important high explosives.

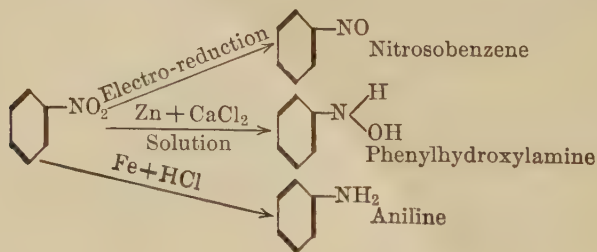
Properties. The nitro compounds are usually pale yellowish liquids or solids, many of them being volatile with steam. Some of them—the higher nitro compounds, such as TNT—are high explosives.



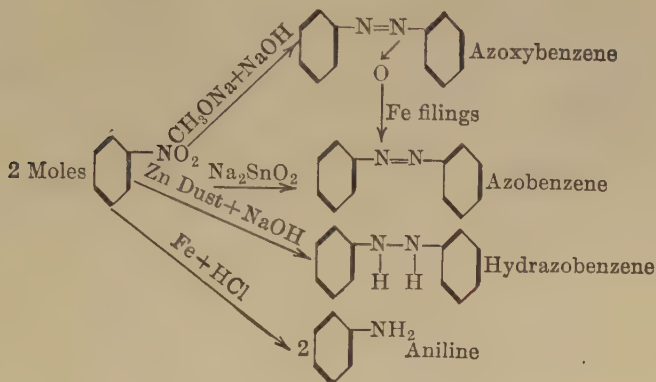
ish oil with an odor resembling that of bitter almonds, for which it is sometimes substituted in perfumes. It is also used in soaps, polishes, and grease (on account of its odor). It is manufactured from benzene on a very large scale for the purpose of preparing aniline, which is an important "dye intermediate."



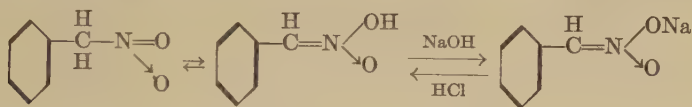
Reduction products of nitro compounds under varying conditions:



Bimolecular Reduction Products:



Aromatic nitro compounds with the NO_2 group in the side chain, such as $\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$, phenylnitromethane, behave like nitroparaffins; for instance, they react as "pseudo acids" and form salts with alkali:



QUESTIONS

- Describe by means of definite examples the methods for the preparation of halogen derivatives of aromatic hydrocarbons. Compare these with the methods used for the preparation of halogenated aliphatic hydrocarbons.
- Discuss the reagents used for, and the conditions which affect the extent of, (a) halogenation; (b) nitration; (c) sulfonation of aromatic hydrocarbons.
- Tabulate the chemical reactions of (a) *n*-heptyl chloride; (b) benzyl chloride; (c) *p*-chlorotoluene.
- How would you ascertain whether a halogen atom is in the nucleus or side chain?
- Indicate the meaning of the following terms: (a) mixed acid; (b) 104 per cent H_2SO_4 ; (c) side chain; (d) halogen carrier; (e) phenylene group; (f) tolyl group; (g) benzyl group; (h) xylyl group.
- Tabulate (a) the monomolecular and (b) the bimolecular reduction products of nitrobenzene, and name the compounds.
- Describe the preparation of the following compounds:

(a) benzene hexachloride	from benzene (give conditions)
(b) bromobenzene	" benzene (give conditions)
(c) <i>p</i> -dichlorobenzene (<i>p</i> -phenylene chloride)	" benzene
(d) benzyl chloride	" benzene (give conditions)
(e) <i>p</i> -chlorotoluene	" benzene (give conditions)

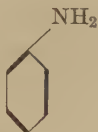
(f) benzal chloride	" benzene (give conditions)
(g) <i>m</i> -benzenedisulfonic acid	" benzene
(h) <i>p</i> -toluenesulfonamide	" benzene
(i) benzenesulfonyl chloride	" benzene
(j) phenol	" benzene
(k) thiophenol	" benzene
(l) <i>m</i> -dinitrobenzene	" benzene
(m) <i>o</i> -nitrotoluene	" benzene
(n) <i>p</i> -aminotoluene	" benzene

CHAPTER XXII

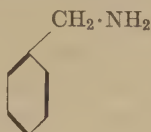
AROMATIC AMINES;¹ DIAZO AND AZO COMPOUNDS

AROMATIC AMINES

The NH_2 group may be attached to the nucleus or to the side chain; e.g.,



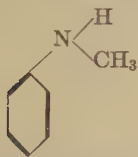
Aminobenzene or phenylamine or aniline



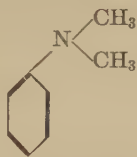
Benzylamine

As might be anticipated, benzylamine shows the general properties of an aliphatic amine, since the NH_2 group is in the side chain.

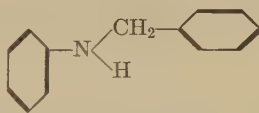
The aromatic amines, like those of the aliphatic series, may be either primary, secondary, or tertiary; e.g.,



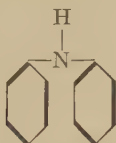
Monomethylaniline
or methylphenylamine
(secondary)



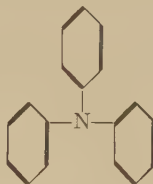
Dimethylaniline
or dimethylphenylamine
(tertiary)



Benzylphenylamine
(secondary)

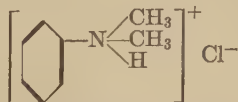


Diphenylamine
or phenylaniline
(secondary)



Triphenylamine
(tertiary)

The aromatic amines are weaker bases than the corresponding aliphatic amines. The primary, secondary, and tertiary amines form salts such as

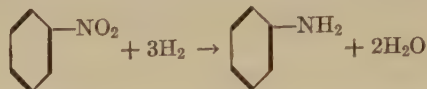


Dimethyl phenyl ammonium chloride
or dimethylaniline hydrochloride

¹ The student should review Chapter XIII on aliphatic amines.

but if all the groups attached to the nitrogen atom are aryl,¹ then no salts are formed. These aryl tertiary amines are not strong enough bases; triphenylamine, for example, does not form a salt with hydrochloric acid.


Preparation. The amines are generally prepared by reducing the nitro compounds; e.g.,



On an industrial scale, iron, steam, and some HCl are used as the reducing agents; in the laboratory, tin or zinc and an acid.

It may be remembered that the aliphatic amines can be prepared by the action of ammonia on the halogen compound:

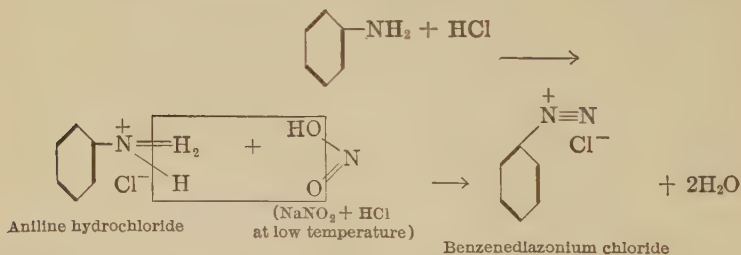


but chlorobenzene, , does not react with ammonia except under pressure.

Reactions with Nitrous Acid. The aliphatic primary amines yield alcohols when treated with nitrous acid; e.g.,

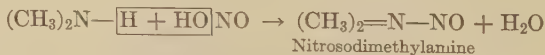


but, with the aromatic primary amines, the reaction is quite different; e.g.,



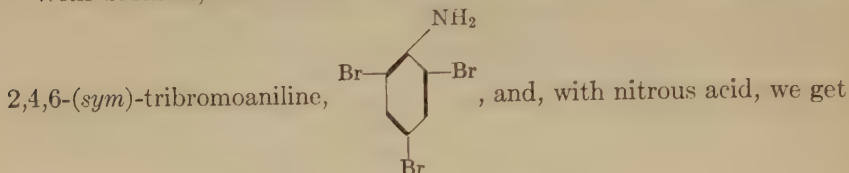
This reaction—the “diazo reaction”—will be taken up later (p. 269).

The secondary amines of the aliphatic series, it will be recalled, yield nitroso compounds; e.g.,

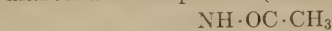


¹ “Aryl” (Ar) groups are C₆H₅ and its homologs, just as “alkyl” (R) groups are the aliphatic groups.

With bromine, and even with bromine water, aniline readily forms

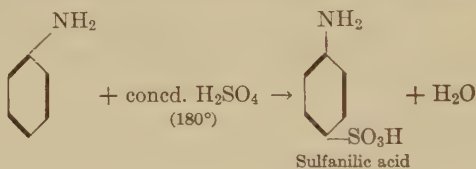


a diazonium compound (diazot reaction, p. 269).

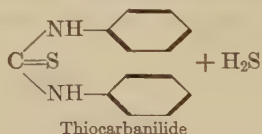


febrin"), is formed when aniline is acted upon by glacial acetic acid or acetic anhydride. It is used in medicine as an analgesic and antipyretic, in the treatment of neuralgia and rheumatism, and in headache powders. The amine group is acetylated to stabilize it while retaining its orienting influence (strongly *o*, *p*). After all chemical modifications of the molecule are completed, a simple hydrolysis by dilute acid restores the free amino group.

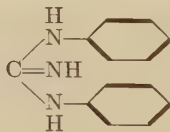
When aniline is heated with H_2SO_4 , sulfanilic acid is produced:



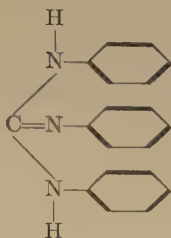
Aniline reacts with carbon disulfide, CS_2 , to form



which is used as an accelerator in the vulcanization of rubber. (By an accelerator we mean a substance which hastens the reaction between the sulfur and the rubber.) It also increases the tensile strength of the vulcanized rubber. Besides thiocarbanilide, the following are the more important accelerators: hexamethylenetetramine (p. 90); diphenylguanidine,



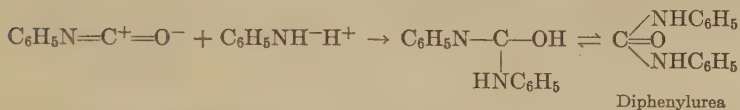
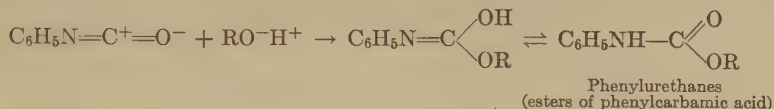
and triphenylguanidine,



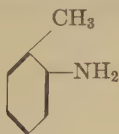
Aniline reacts with carbonyl chloride (phosgene) to yield phenyl isocyanate:



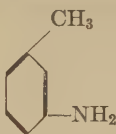
This reagent is useful for the identification of alcohols and amines, which form crystalline addition derivatives of characteristic melting point:



Of the three **toluidines** or aminotoluenes,



o-Toluidine or *o*-aminotoluene

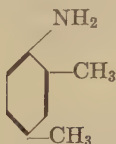


m-Toluidine

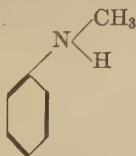


p-Toluidine

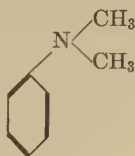
the *o*- and *p*- may be obtained by the reduction of the corresponding nitro compounds. A few other amines are:



m-Xylidine or 1,2,4-xylidine



Methylaniline



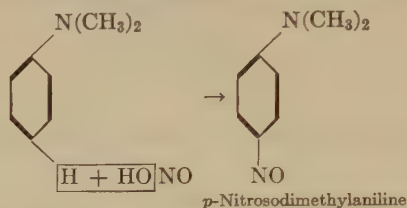
Dimethylaniline

The last two are manufactured by heating aniline and methanol, or aniline and methyl chloride under pressure, the one or the other amine being obtained, depending upon the ratio of the reacting substances used.

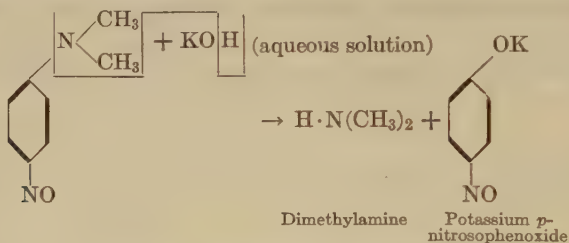
Both the methylaniline and the dimethylaniline are used extensively in the manufacture of dye intermediates and dyes.

Diethylaniline, $C_6H_5N(C_2H_5)_2$, produced by the action of aniline and ethyl chloride under pressure, is also used as a dye intermediate.

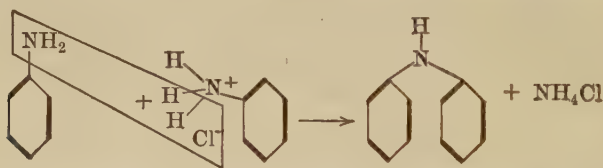
Nitrous acid reacts with dimethylaniline as follows:



the product being used in the manufacture of dyes and for the preparation of pure dimethylamine:

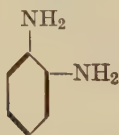


Diphenylamine, or phenylaniline, is manufactured by heating aniline with aniline hydrochloride around 240° in an autoclave (under pressure).

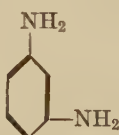


It is added to smokeless powder to increase its stability, and it is also used as a test for nitric acid and nitrates, and in the manufacture of dyes. Adamsite (p. 256) is made by heating diphenylamine hydrochloride with As_2O_3 .

The diaminobenzenes,



o-Diaminobenzene
or
o-phenylenediamine



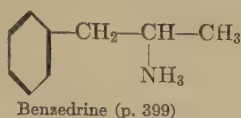
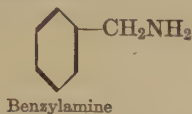
m-Phenylenediamine



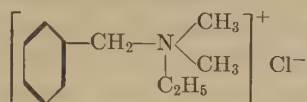
p-Phenylenediamine

are known as the "diamines." The *m*- and *p*-compounds are used very extensively in the manufacture of dyestuffs. (The C_6H_4 group—divalent—is known as the "phenylene" group.)

The aryl aliphatic amines, in which the amino N is in a side chain, are, of course, aliphatic amines and much stronger bases than the aromatic amines.



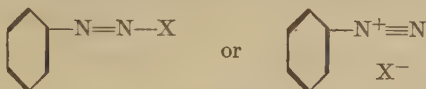
Quaternary ammonium compounds made from such amines are of use as antiseptics and detergents (known as "invert" soaps since, in this case, the anion is the active fragment, instead of the cation as in soaps and sulfate detergents); for example,



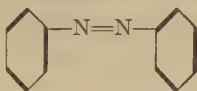
DIAZO AND AZO COMPOUNDS

"Azote" is the French word for nitrogen. "Diazo," therefore, indicates *two* nitrogens.

A diazo compound has one aryl group attached to one nitrogen:

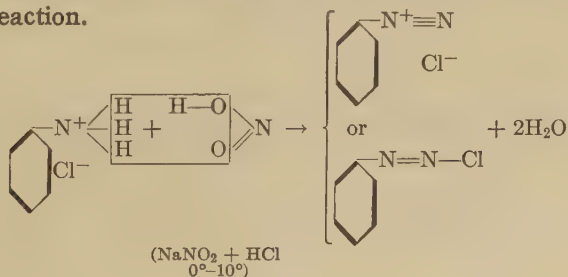


An azo compound has two aryl groups attached to two nitrogen atoms:

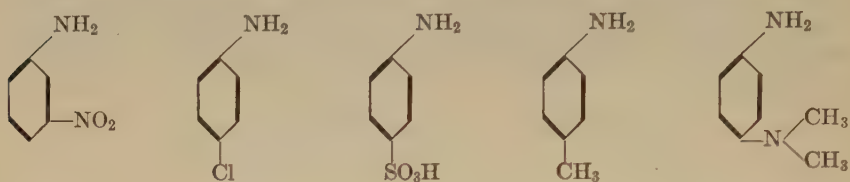


The diazo and azo substances are an extremely important class of organic compounds. They have played a very important part in the development of synthetic and industrial organic chemistry, especially in the manufacture of dyestuffs. These facts will be appreciated as we proceed.

Diazo Reaction.



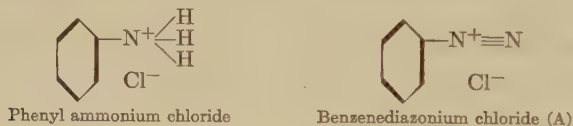
In the place of the phenyl group we may use any other substituted aryl groups, such as are illustrated in the following compounds:



as well as the naphthalene group (p. 322), containing the NH_2 attached to the ring; so that the reaction is of the widest possible application.

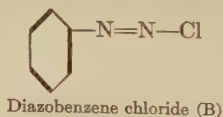
The action of nitrous acid on a primary aromatic amine, whereby a diazonium compound is formed, is known as *diazotization*.

The diazo compounds in solution are highly unstable at ordinary temperatures. As a rule, they are not prepared in the dry state, for they are more or less unstable and explosive; but a few can be prepared in this way when mixed with an inert material. They are usually soluble in water and show many properties analogous to the ammonium salts, such as conductivity and salt formation. The structure is written with this analogy in mind; e.g.,

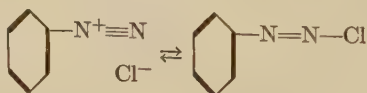


where one N in (A) has an ammonium structure. Compounds of type (A) are known as "diazonium," the ending *-ium* suggesting the ending in "ammonium." Benzenediazonium chloride may be looked upon as phenyl ammonium chloride wherein the three hydrogens are replaced by one nitrogen.

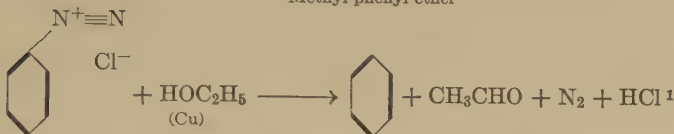
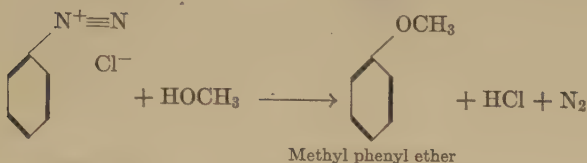
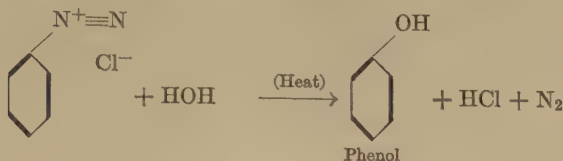
Compounds of type (A), like the ammonium compounds, show salt-like properties. In some reactions, however, the diazotized product does not show saltlike properties, hence (A) is also written:



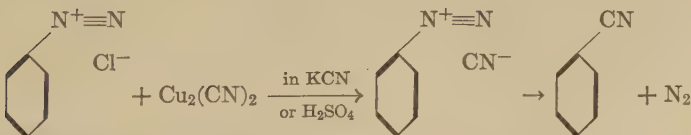
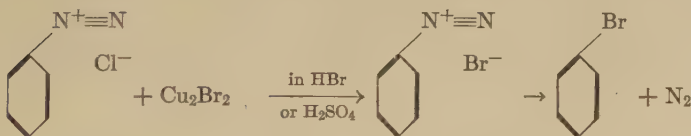
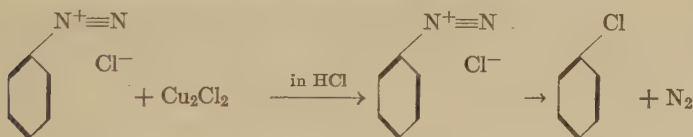
We probably have both (A) and (B) present in compounds of the diazo type:



Many types of aromatic compounds are prepared from these diazonium or diazo compounds; e.g.,



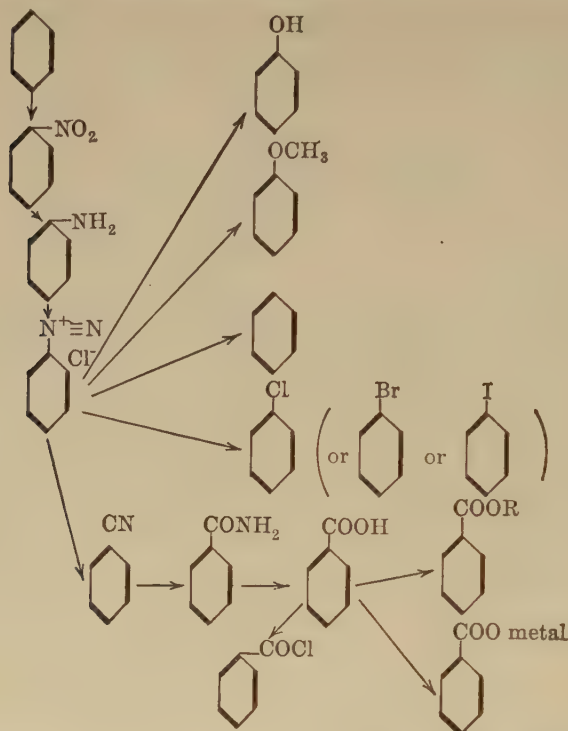
The following are known as *Sandmeyer* reactions:



Copper powder may be used instead of the cuprous salts.

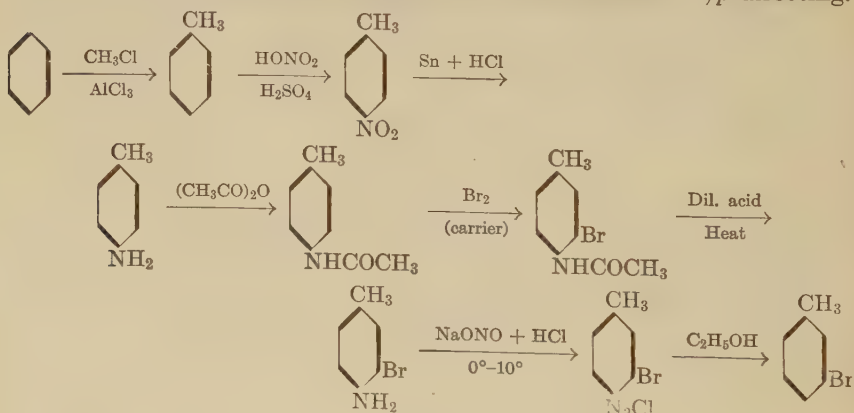
We may summarize these reactions to show the preparation of various types of aromatic compounds:

¹ Other reagents suitable for this reduction are $\text{H}\cdot\text{CHO} + \text{NaOH}$ or $\text{SnCl}_2 + \text{NaOH}$.

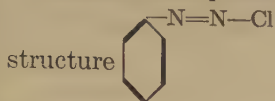


which gives an idea of the wide applicability which these diazonium compounds possess.

One of their uses in synthesis is based on the fact that the diazonium group, rather easily obtained from an amino group, can be conveniently replaced by hydrogen; this enables us to use the *o*-, *p*-directing influence of —NH_2 and to remove it afterwards, for example in the synthesis of *m*-disubstituted benzenes in which both substituents are *o*-, *p*-directing.

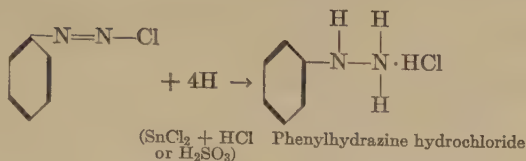


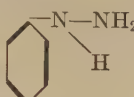
We must now proceed to reactions which are better explained by the



Upon partial reduction, the following reaction

takes place:

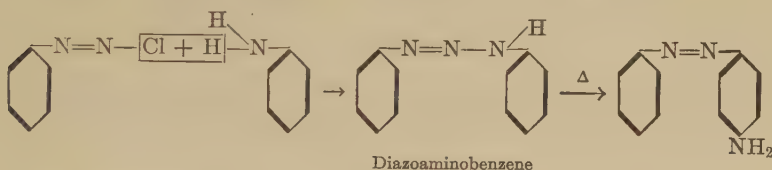


and the base, **phenylhydrazine**,  , may be obtained by the addition of NaOH. (Hydrazine is H₂N—NH₂.)

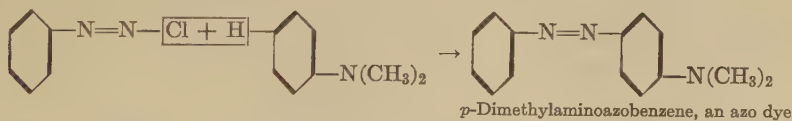
Phenylhydrazine, a poisonous liquid, has been used very extensively by Fischer and others in determining the structure of sugars. It is used in the identification of sugars, in tests for aldehydes and ketones, and in the manufacture of antipyrine (p. 334) and of various dyestuffs.

2,4-Dinitrophenylhydrazine is very frequently used also for the preparation of derivatives of carbonyl compounds.

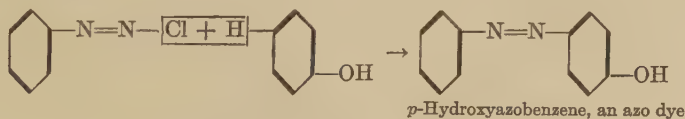
Diazobenzene chloride may be "coupled" with aniline (in neutral or weak acid solution) thus:



and with dimethylaniline:



and with phenol:

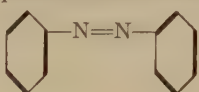


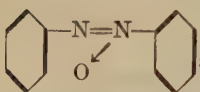
—reactions which are much better explained on the basis of a "diazo" than on that of a "diazonium" configuration.

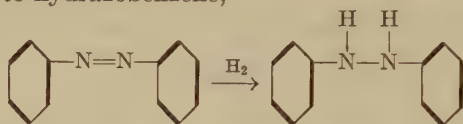
Reactions of the type just given are of great importance in the manufacture of azo dyes (p. 351).

Azo dyes, and other azo compounds, are split by reduction ($\text{SnCl}_2 + \text{HCl}$) into two primary amines. This method is used to prepare some primary aromatic amines.

The azo compounds are far more stable than the diazo compounds.

Azobenzene, , is prepared by distilling azoxybenzene,

, with iron filings; or by the action of an alkaline solution of stannous chloride on nitrobenzene. It may be reduced by zinc and acetic acid to hydrazobenzene,



which, when boiled with strong HCl , undergoes an intramolecular rearrangement into *p,p'*-diaminodiphenyl, better known as **benzidine**,



which is an important dye intermediate. Benzidine is also used in a test for blood.

QUESTIONS

1. Compare the methods of preparation of aliphatic and aromatic amines.
2. Compare the reactions of aliphatic and aromatic amines with nitrous acid.
3. Describe the preparation of the following compounds:

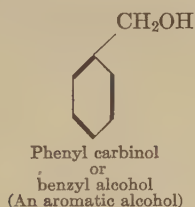
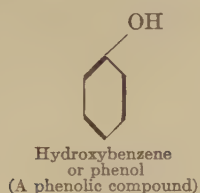
(a) dimethylaniline	from benzene
(b) <i>p</i> -toluidine	" benzene
(c) thiocarbanilide	" benzene
(d) sulfanilic acid	" benzene
(e) diphenylamine	" benzene
(f) phenol	" aniline
(g) <i>o</i> -chlorotoluene	" <i>o</i> -nitrotoluene
(h) benzoic acid	" aniline
(i) phenylhydrazine	" aniline
(j) azobenzene	" nitrobenzene
(k) <i>p</i> -dimethylaminoazobenzene	" nitrobenzene
(l) <i>p</i> -hydroxyazobenzene	" nitrobenzene
(m) <i>p</i> -nitrosodimethylaniline	" nitrobenzene
(n) benzidine	" nitrobenzene
(o) benzene	" <i>o</i> -nitrotoluene
(p) acetanilide	" nitrobenzene
(q) <i>m</i> -phenylenediamine	" benzene

CHAPTER XXIII

AROMATIC ALCOHOLS, PHENOLS, AND ETHERS


We have already pointed out that in aromatic compounds substitution may occur either in the side chain or in the nucleus, and that the products obtained when substitution takes place in the side chain are quite different from those obtained when substitution takes place in the nucleus.

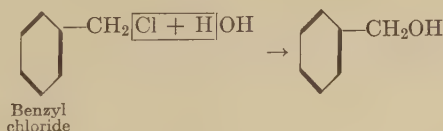
We have seen, in the amines, for example, how the NH_2 group may be attached either to the nucleus or to the side chain. This is equally true of the OH group. Where the OH is attached to the nucleus, we have a phenol, and where it is attached to the side chain we have an aromatic alcohol; e.g.,



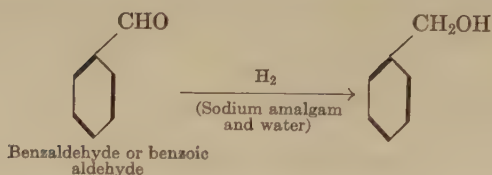
In the aromatic alcohols, the OH group is attached to an alkyl residue or side chain; the properties of these compounds, therefore, are closely analogous to those of the aliphatic alcohols. (See Chapter V.)

AROMATIC ALCOHOLS

Benzyl alcohol, , or phenyl carbinol, occurs as esters in balsam of Peru and Tolu, storax resin, in oils of flowers, etc. It may be obtained as follows:



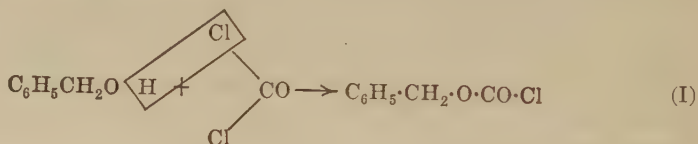
or



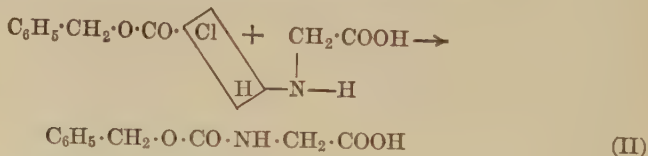
It is used in perfumery, and in medicine as a local anesthetic.

Bergmann has made use of benzyl alcohol in the preparation of polypeptides. His method of forming polypeptides is a very important one, and may be illustrated as follows.

Benzyl alcohol can be condensed with phosgene to give the acid chloride of benzylcarbonic acid:



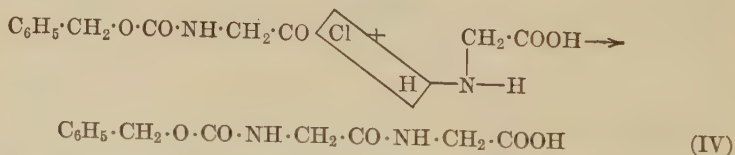
I can be condensed with an amino acid—we shall take glycine for the sake of simplicity—to yield the corresponding carbobenzyloxy derivative:



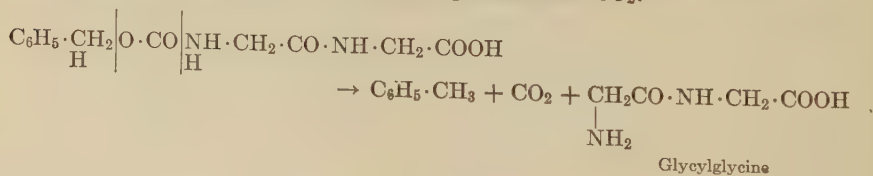
II is converted to its acid chloride with PCl_5 :



III can be condensed with another amino acid—we shall again take glycine for the sake of simplicity:

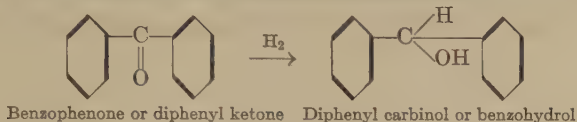



By catalytic hydrogenation (in the presence of palladium black) the carbobenzyloxy residue is removed from IV, liberating toluene and CO_2 :




By repeating these processes, tri- and tetrapeptides, etc., can be obtained. Obviously, also, amino acids other than glycoch (glycine) can be used.

Diphenyl carbinol, or benzohydrol, is a secondary alcohol, and may be prepared by reducing the corresponding ketone.




Cinnamyl alcohol, , present in storax, has an odor like that of hyacinth. It is used in perfumery.

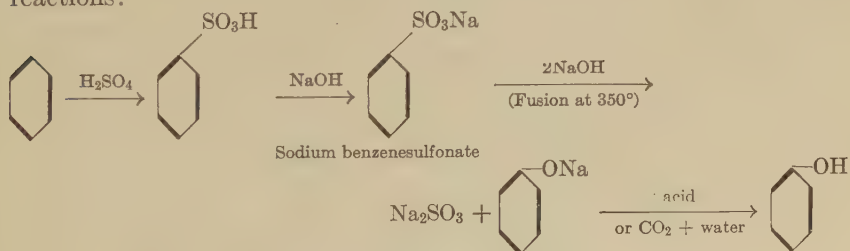
Phenylethyl alcohol, , is present in oil of rose and is used in perfumes. It is prepared by the interaction of benzene and ethylene oxide (*Friedel-Crafts*).

Aromatic alcohols can be prepared by the same general methods as the aliphatic alcohols, such as the *Grignard* synthesis. The *Cannizzaro* reaction (p. 286) offers another useful method of preparation.

PHENOLS

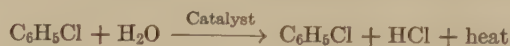
The aromatic alcohols, like those of the aliphatic series, are neutral bodies; but when the OH enters the ring we get a phenolic compound, which is a very weak acid. The most important among these phenolic

compounds is **phenol**, , or hydroxybenzene, or carbolic acid. It is present in wood tar and coal tar (see chart facing p. 236), from which much of it is obtained. It is manufactured by the following series of reactions:

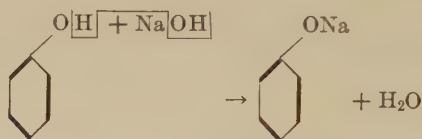


It may also be prepared by the diazo reaction.

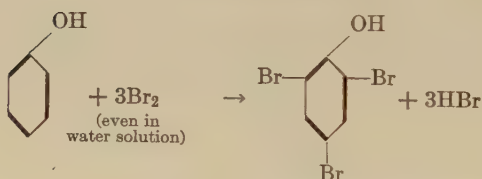
Another method for the preparation of phenol is by the hydrolysis of chlorobenzene with Na_2CO_3 solution under high pressure. A modification of this method involves the use of HCl , produced in the hydrolysis of chlorobenzene, to make more chlorobenzene, thus keeping the chlorine in constant circulation:



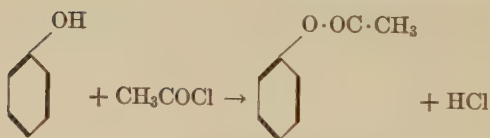
Properties. Phenol is a very weak acid, weaker than carbonic acid. It is very corrosive and poisonous. Some of its general reactions may be illustrated by the following:



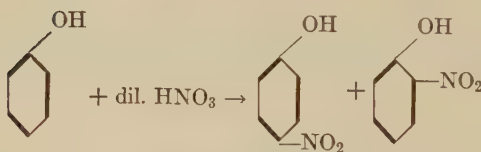
Sodium phenoxide



2,4,6 (*sym*)-Tribromophenol

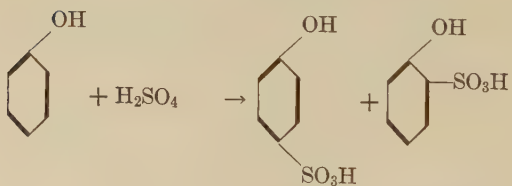


Phenyl acetate (an ester)



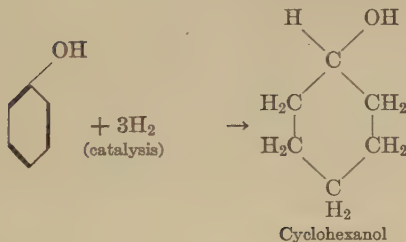
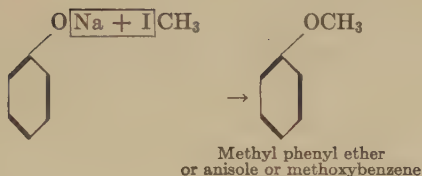
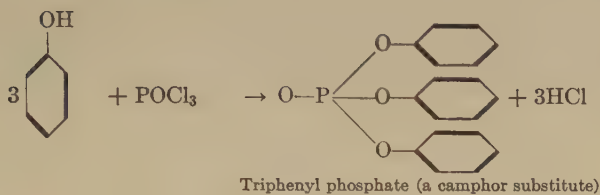
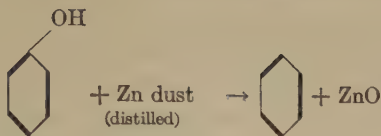
p-Nitrophenol

o-Nitrophenol



p-Phenolsulfonic acid

o-Phenolsulfonic acid

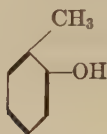


Phenol gives a violet color with ferric chloride. It is a colorless, crystalline substance which becomes liquid upon the addition of 15 per cent of water. It is a powerful antiseptic, disinfectant, and germicide, and is used to a certain extent (in 3 per cent solution) as a dressing for wounds, for disinfecting surgical instruments, rooms, etc.

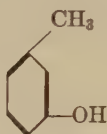
Phenol is used in the manufacture of plastics, explosives, dyes, developers, and various medicinals. It combines with formaldehyde to produce resinous materials or plastics, some of which were among the earliest of such products to be of practical value. These products—known as Bakelite, etc.—vary in properties, for the particular type of resin obtained will depend upon the exact method employed in its preparation. Pure phenol and pure formaldehyde react very slowly, even when heated, but in the presence of catalytic agents, particularly bases—ammonia seems to be used in many cases—the action is accelerated. Where ammonia is employed, it is believed that the first reaction

is between the formaldehyde and the ammonia, forming hexamethylenetetramine (p. 90), which then combines with phenol, forming a resin, the chemical composition of which is not clear. This resin undergoes further changes when heated. It then becomes infusible and less soluble. The raw Bakelite, for example, is both soluble and fusible, but when heated it becomes insoluble, infusible, very hard, strong, and resistant. Bakelite is used in molding materials, varnishes, enamels, lacquers, cements, pipe stems, cigar holders, handles, insulating substances, etc.

Cresols.



o-Hydroxytoluene or *o*-cresol

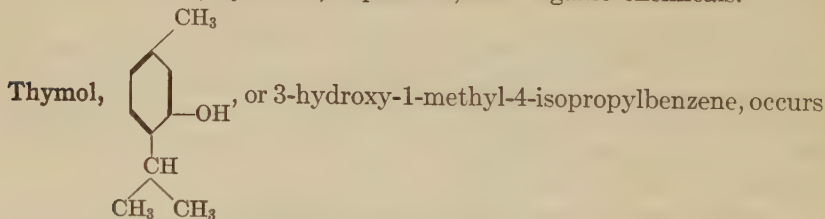


m-Cresol

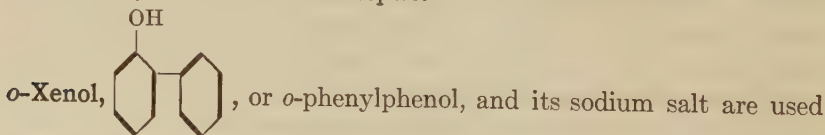


p-Cresol

All three cresols are present in coal tar and in wood tar, and all three act as antiseptics. A mixture of the higher homologs containing two or more methyl groups is known as "cresylic acid" or "tricresol." The properties of these cresols are, in general, similar to those of phenol. The cresols have greater germicidal power than phenol and are less poisonous. They are slightly soluble in water and are rendered more soluble by the addition of soap. Preparations such as Lysol, Creolin, and Phenoco contain cresols. Cresols are also used for the manufacture of synthetic resins, dyestuffs, explosives, and organic chemicals.

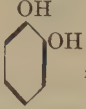


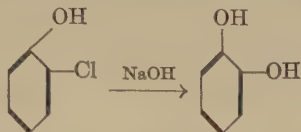
in oil of thyme, mint, and other essential oils, and is an important antiseptic. It is very often used in the treatment of hookworm and to preserve urine. Diiododithymol (prepared from thymol and iodine), like iodoform, is used as an antiseptic.



as germicides and fungicides.

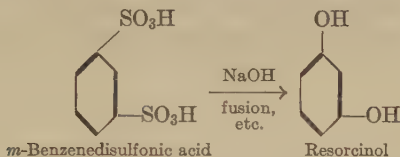
POLYHYDROXY PHENOLS

Catechol, or pyrocatechol, , a product of the destructive distillation of "catechu," an extract from the wood of *Acacia catechu*, is prepared from resins by fusing them with KOH, or from *o*-chlorophenol by hydrolysis:



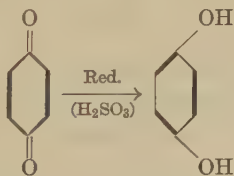
It is used in the manufacture of adrenaline and guaiacol.

Resorcinol, or resorcin, or *m*-dihydroxybenzene, is prepared thus:



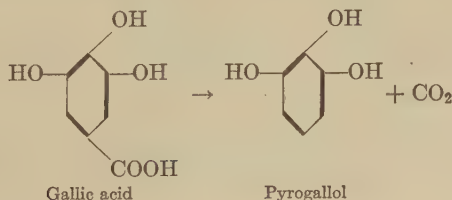
It is used as an antiseptic and in the preparation of dyestuffs.

Hydroquinone, or quinol, or *p*-dihydroxybenzene, is prepared from *p*-benzoquinone (p. 290) by reduction:



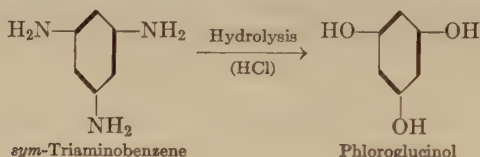
It is used as a photographic developer (that is, as a mild reducing agent, it being converted into benzoquinone).

Of the three trihydroxybenzenes, **pyrogallol** (or pyrogallie acid) is obtained by heating gallic acid:



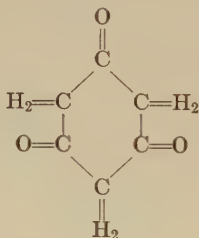
It is a strong reducing agent and absorbs oxygen in alkaline solution—a property utilized in estimating oxygen in gas mixtures. Pyrogallol is also used as a photographic developer and in the manufacture of dye-stuffs.

Phloroglucinol, or *sym*-(1,3,5)trihydroxybenzene, may be prepared from the corresponding triamino compound:

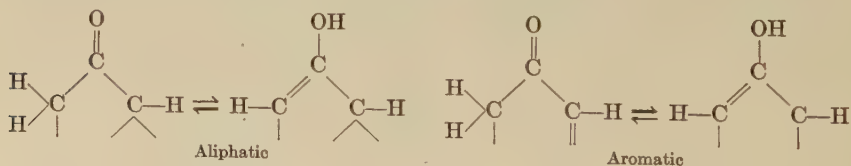


It occurs in combination in the glucoside phloridzin.

The behavior of phloroglucinol towards reagents is worthy of discussion. That it is a trihydroxy compound is shown by the fact that it forms a triacetyl derivative with acetic anhydride. On the other hand, it forms a trioxime with hydroxylamine, indicating a ketonic structure:

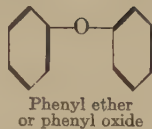
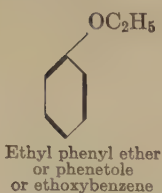
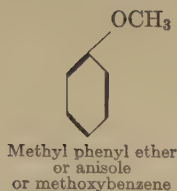


Where, under certain conditions, the same compound may exist in two different forms, we have **tautomerism**. (This is to be distinguished from isomerism, where we have two different compounds with the same molecular formula.) From this point of view, we may compare aliphatic carbonyl compounds, in which the keto form is the normal, stable form, with corresponding aromatic compounds in which, of course, the enolic phenol form is by far the more prevalent.

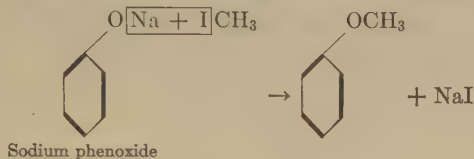


Phloroglucinol is used for the determination of furfural—a test based upon the production of a red color.

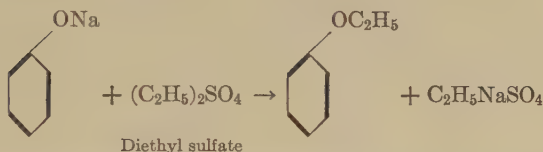
ETHERS ¹



Ethers of the type of **anisole** and **phenetole** are produced thus:



or



Diphenyl ether is prepared by heating phenol with zinc chloride and is also a by-product in the manufacture of phenol from chlorobenzene:



It has a geranium-like odor, and is used as a heat-transfer agent, like diphenyl.

These ethers are used in synthetic perfumes.

QUESTIONS

1. Give the structural formulas, chemical names, methods of preparation, and commercial uses of (a) phenol; (b) resorcinol; (c) cresols; (d) pyrogallol; (e) phloroglucinol.
2. Discuss the preparation and uses of Bakelite resins.
3. Write structural formulas for (a) benzyl alcohol; (b) *sym*-tribromophenol; (c) catechol; (d) hexylresorcinol; (e) quinol; (f) 1,3-dihydroxybenzene; (g) adjacent trihydroxybenzene; (h) *unsym*-trihydroxybenzene; (i) thymol; (j) diphenyl carbinol; (k) phenetole; (l) methyl phenyl carbinol; (m) cinnamyl alcohol.
4. Starting with benzene, write equations for the preparation of (a) benzophenone; (b) phloroglucinol; (c) anisole; (d) phenetole; (e) diphenyl ether; (f) benzyl alcohol; (g) phenylethyl alcohol.
5. Starting with benzene, outline a mode of procedure for the preparation of the three dihydroxybenzenes.


¹ The student is advised to review Chapter VI.

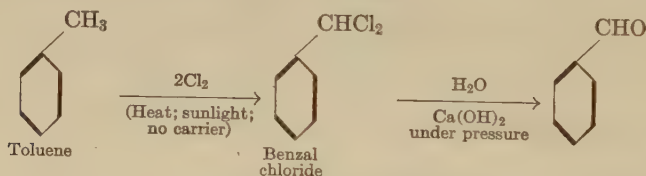
CHAPTER XXIV

AROMATIC ALDEHYDES, KETONES,¹ AND QUINONES

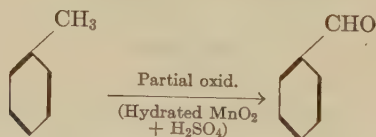
The aromatic aldehydes and ketones contain the $\text{—C}\begin{smallmatrix} \text{O} \\ \text{//} \\ \text{H} \end{smallmatrix}$ and >C=O groups, respectively (like the aliphatic compounds). The quinones have no analogs in the aliphatic series.

AROMATIC ALDEHYDES

Benzaldehyde, , or benzoic aldehyde, or artificial oil of bitter almonds, is the most important aromatic aldehyde. This compound may be prepared in several ways:




or

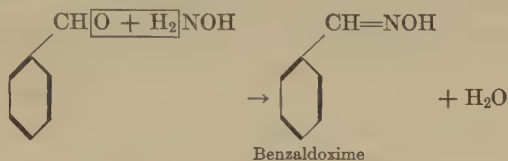


Benzaldehyde occurs in bitter almonds, the kernels of fruits, etc. In bitter almonds, the aldehyde is present in the form of a glucoside (amygdalin). An enzyme present in amygdalin, and known as emulsin, hydrolyzes the glucoside into glucose, hydrogen cyanide, and benzaldehyde. This hydrolysis may also be brought about by means of acids. Benzaldehyde is used extensively in flavoring extracts and perfumes, in the manufacture of dyes, and in the preparation of various organic compounds.

¹ The student should review Chapter VII on the aliphatic aldehydes and ketones.

Properties. Many of the properties of benzaldehyde resemble those of the aliphatic aldehydes. When exposed to air, it is oxidized to the

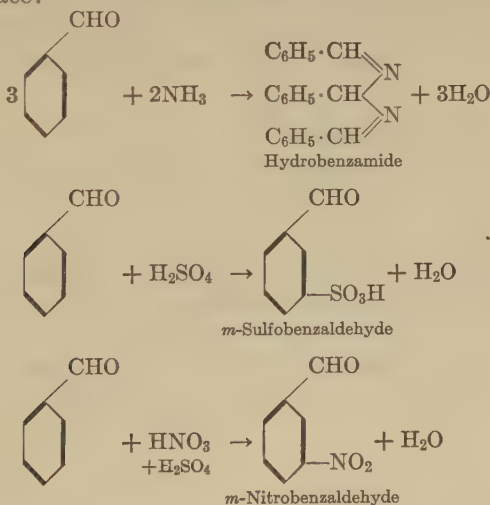
corresponding benzoic acid, ; it reduces ammoniacal silver nitrate solution; it forms addition compounds with NaHSO_3 and HCN ; and reacts with hydroxylamine and phenylhydrazine to form oximes and a phenylhydrazone, respectively.



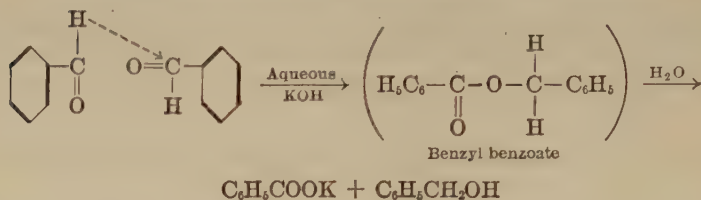
Two forms, stereoisomeric forms (p. 108), are known:



With ammonia and with sulfuric and nitric acids the following reactions take place:



In the presence of alkali, benzaldehyde undergoes a simultaneous oxidation and reduction (disproportionation) with the formation of one molecule of each of the corresponding alcohol and acid.



This type reaction, known as the *Cannizzaro* reaction, can be applied to those aldehydes in which there is no hydrogen attached to the α -carbon atom; for example, formaldehyde and benzaldehyde.

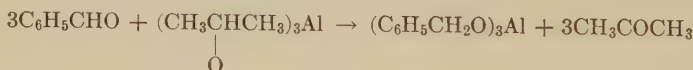
The *Cannizzaro* reaction provides a convenient means of preparing aromatic alcohols, even though the theoretical yield, calculated from the aldehyde, is only 50 per cent. The aromatic aldehydes are relatively inexpensive materials, and the alcohols prepared from them are free of chlorine and other substances which would render them unsuitable for use in perfumes and similar products.

A more economical preparation of alcohols can be effected by a "crossed" *Cannizzaro* reaction, in which a cheaper aldehyde (with no α -hydrogen), such as formaldehyde, functions as reducing agent; for example:

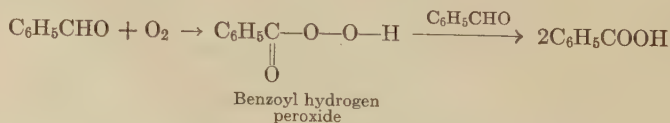


Another useful disproportionation reaction uses aliphatic alcohols, in the form of metallic salts [for example, aluminum isopropoxide, $(\text{CH}_3\text{CH}(\text{CH}_3)_2)_3\text{Al}$], to reduce the aromatic aldehyde, the alcohol being


oxidized to a carbonyl compound:




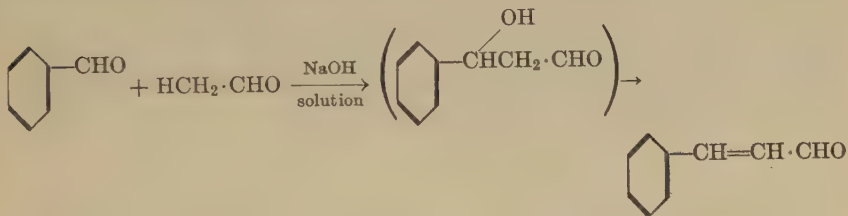
Aromatic aldehydes undergo oxidation very readily on standing, the oxygen of the air being the oxidizing agent. This *autooxidation* accounts for the presence of acids in the common samples of aldehydes. The formation of an intermediate peroxide can be demonstrated by the oxidation of substances other than the aldehyde itself (for example, $\text{I}^- \rightarrow \text{I}$):



Some peroxides can be isolated; they are active oxidizers.

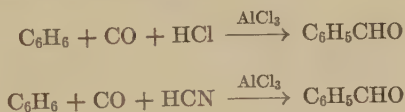
Phenylacetaldehyde, , has a hyacinth odor and is used in perfumes.

Cinnamaldehyde, , or β -phenylacrylaldehyde, is the chief constituent of oil of cinnamon; it is used in perfumery. It can be synthesized by condensing benzaldehyde with acetaldehyde:




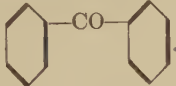
This is an aldolization, generally known as a *Claisen* condensation.


Aromatic aldehydes can be prepared from hydrocarbons by a modification of the *Friedel-Crafts* synthesis (*Gattermann*):

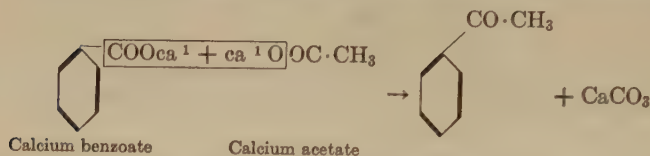


AROMATIC KETONES

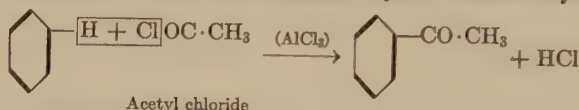
The aromatic ketones may be divided into those containing aryl and alkyl groups, e.g., , and those in which both groups are

aryl, e.g., .

Acetophenone, , or methyl phenyl ketone, or "hypnone," is used as a soporific. It may be prepared as follows:



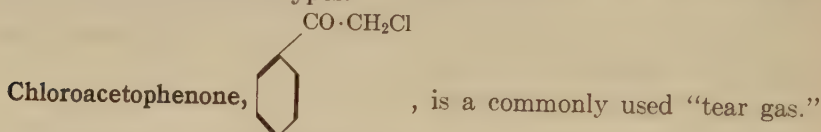
but on a commercial scale it is prepared by a *Friedel-Crafts* synthesis.



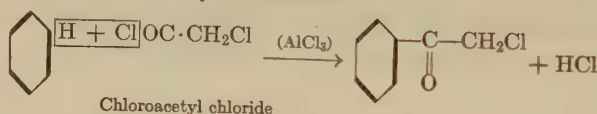
Here acetic anhydride may be used in place of acetyl chloride, since the former reacts with AlCl_3 to form acetyl chloride.



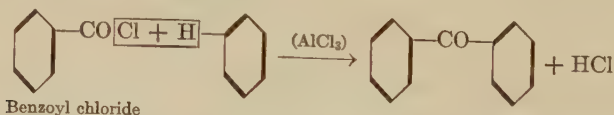
These two methods are of general application in the preparation of aromatic ketones of both types.



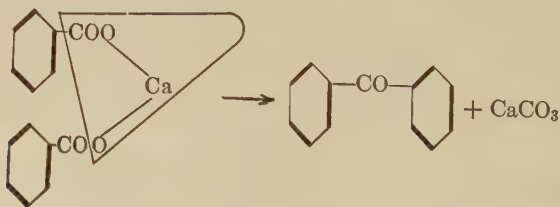
It is made by a *Friedel-Crafts* reaction:



Benzophenone, $\text{C}_6\text{H}_5\text{CO} \cdot \text{C}_6\text{H}_5$, or diphenyl ketone, may be prepared by another *Friedel-Crafts* reaction:

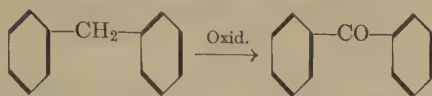


Benzophenone can also be prepared by the distillation of calcium benzoate:

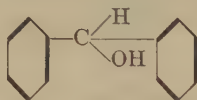


¹ ca here indicates $\frac{1}{2}\text{Ca}$.

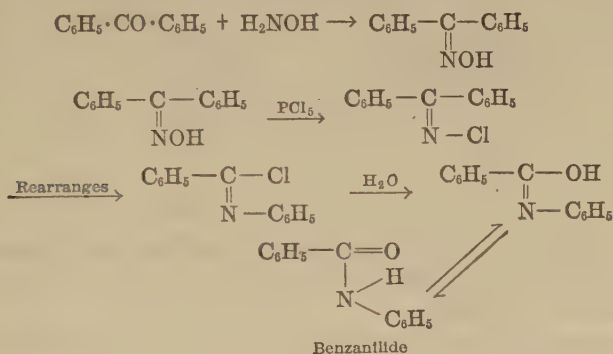
or by the oxidation of diphenylmethane:



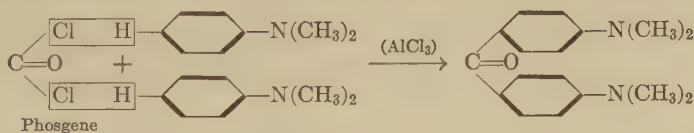
Benzophenone, when reduced, forms benzohydrol, or diphenyl carbinol:



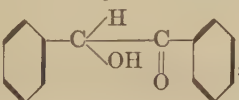
When benzophenone is treated with hydroxylamine, benzophenone oxime is obtained. If this compound is treated with PCl_5 or acetyl chloride and then with water, benzanilide is produced. This is a general reaction for ketoximes, known as the *Beckmann* rearrangement. These changes may be illustrated by the following scheme:



Michler's ketone, or *p,p'*-tetramethyldiaminodiphenyl ketone, is manufactured as follows:



It is an important dye intermediate.

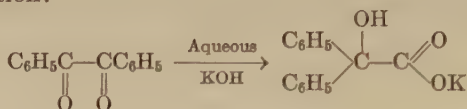
Benzoin, , is obtained from benzaldehyde when it

is treated with alcoholic KCN solution, two molecules of the aldehyde condensing.

Such *acyloins* are known in the aliphatic as well as in the aromatic series. Benzoin is oxidized easily by air to benzil, $\text{C}_6\text{H}_5\text{C}-\text{CC}_6\text{H}_5$, an



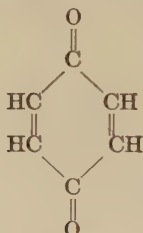
α -diketone. This compound undergoes a rearrangement to benzilic acid in alkaline solution:



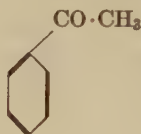
(Compare the pinacol-pinacolone rearrangement, p. 86.)

QUINONES

The CO group in an aromatic ketone is not part of the ring. Quinones are aromatic compounds in which the CO is part of the ring; e.g.,



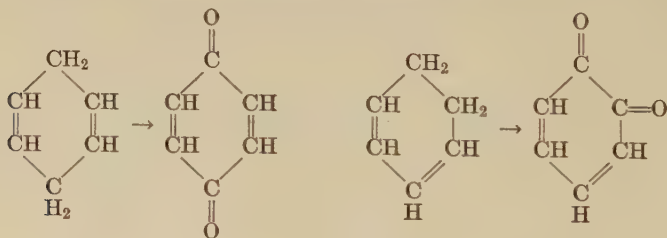
A quinone






A ketone

When the two CO groups are in the *p*-position with respect to one another, we get *p*-quinones, and when in the *o*-position, *o*-quinones. No *m*-quinones are known.

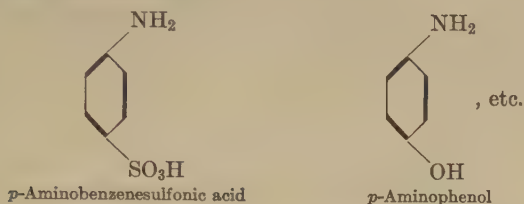
The quinones may be regarded as derivatives of dihydrobenzenes in which two CH_2 groups are replaced by two CO groups:



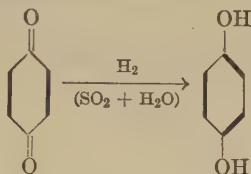
Quinone, , or *p*-benzoquinone, may be prepared by the oxidation

of hydroquinone  \rightarrow , or by the oxidation of aniline with

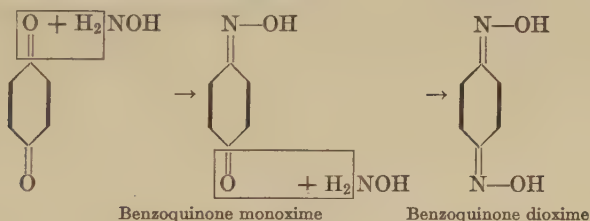
$\text{Na}_2\text{Cr}_2\text{O}_7 + \text{H}_2\text{SO}_4$, or by the oxidation of amino and hydroxy compounds of the *p*-series such as



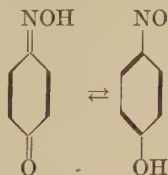
Benzoquinone is a yellow, crystalline solid, volatile with steam and possessing a pungent odor. It is reduced to hydroquinone:



Quinone forms mono- and dioximes:

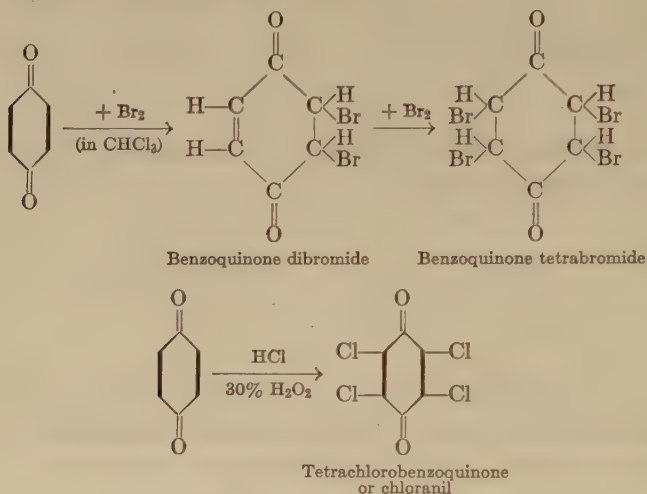


Benzoquinone monoxime is identical with *p*-nitrosophenol, prepared from phenol by substitution:



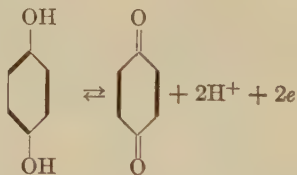
In this case the *benzenoid* and *quinoid* structures are tautomers. Syntheses and reactions of quinones illustrate this same structural convertibility.

Benzoquinone reacts with halogens:

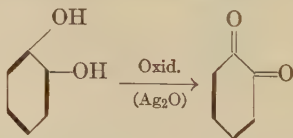


The halogen compounds shown are addition products within the ring—a fact which suggests that these quinones are quite unlike benzene derivatives—or substitution products.

When hydroquinone is heated with ferric chloride, quinhydrone precipitates. Quinhydrone may be looked upon as a molecular complex of one mole of quinone and one of hydroquinone, $C_6H_4(OH)_2 \cdot C_6H_4O_2$. Quinhydrone is used very extensively in pH determinations; it forms an oxidation-reduction system which can be used as a standard half-cell of constant pH:



o-Benzoquinone is prepared from catechol by oxidation:



The structure of quinones has been used to explain the chemistry of dyestuffs and the relationship between color and chemical structure (p. 348).

QUESTIONS

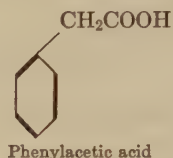
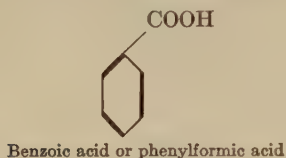
1. Write structural formulas for (a) phenylacetaldehyde; (b) cinnamaldehyde; (c) β -phenylacrylaldehyde; (d) benzophenone; (e) *p*-benzoquinone; (f) *syn*-benzaldoxime; (g) acetophenone; (h) chloroacetophenone; (i) benzoyl chloride; (j) diphenyl ketone; (k) benzamide; (l) acetanilide; (m) benzanilide; (n) hydroquinone; (o) *p*-benzoquinone dioxime; (p) Michler's ketone; (q) *p,p'*-tetramethyldiaminodiphenyl ketone; (r) tetrabromobenzoquinone; (s) benzoquinone tetrabromide; (t) chloranil; (u) acetylbenzene.
2. Write equations for the preparation of the following compounds:

(a) benzaldehyde	from toluene
(b) cinnamaldehyde	" benzaldehyde
(c) Michler's ketone	" aniline
(d) methyl phenyl ketone (acetophenone)	" benzene
(e) quinone	" aniline
(f) tetrachlorobenzoquinone	" aniline
(g) hydroquinone	" benzene
(h) <i>o</i> -benzoquinone	" phenol
(i) benzophenone	" benzoic acid
(j) benzaldoxime	" benzene
(k) benzanilide	" benzoic acid
(l) chloroacetophenone	" benzene
(m) benzanilide	" benzoyl chloride
(n) benzoquinone monoxime	" quinol
(o) benzyl alcohol	" benzaldehyde
3. A ketoxime is treated with PCl_5 (in ether). Hydrolysis of the resulting product yields *o*-nitroaniline and *p*-bromobenzoic acid. Write two possible structures for the original ketone.

CHAPTER XXV

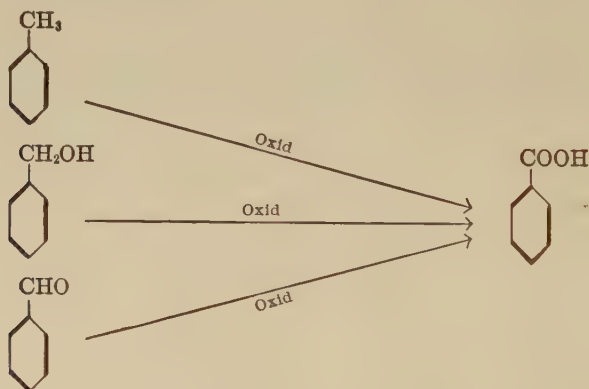
AROMATIC ACIDS AND THEIR DERIVATIVES ¹

The aromatic acids contain the COOH group attached directly to the ring or to the side chain; e.g.,

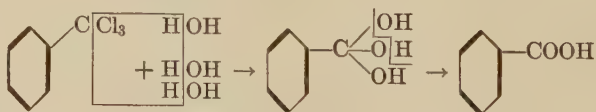


Many of the aromatic acids occur in nature (either in the free state or in the form of esters). We shall select benzoic acid as representative of the group.

Benzoic acid may be prepared by the oxidation of toluene, benzyl alcohol, or benzaldehyde:

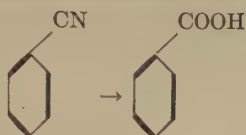


Because of the large use of toluene for explosives, benzoic acid is made on an industrial scale by passing a mixture of phthalic anhydride (p. 299) and an excess of steam over zinc oxide at 450° C. It is also made by the hydrolysis of benzotrichloride:



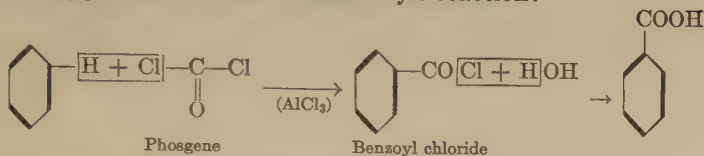
¹ The student should review Chapters VIII, IX, XI, and XII.

by the hydrolysis of the corresponding cyanide:

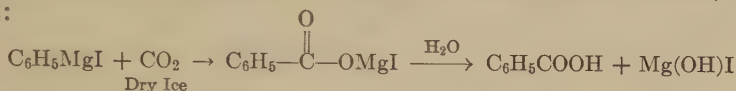


Benzonitrile or cyanobenzene

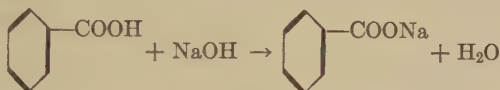
or by the application of the *Friedel-Crafts* reaction:



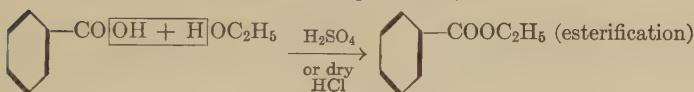
Benzoic acid may also be produced with the *Grignard* reagent, using CO_2 :



Benzoic acid occurs (as the free acid or as the ester) in gum benzoin, resins, balsam of Tolu and Peru, berries, etc. The free acid is generally purified by sublimation. Its properties are similar to those of compounds containing, on the one hand, a benzene nucleus, and on the other hand, a carboxyl group. Some of its reactions may be summarized as follows:



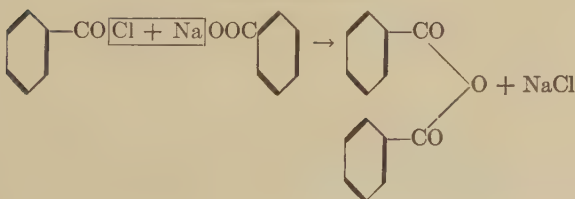
Sodium benzoate
(used as a food preservative)



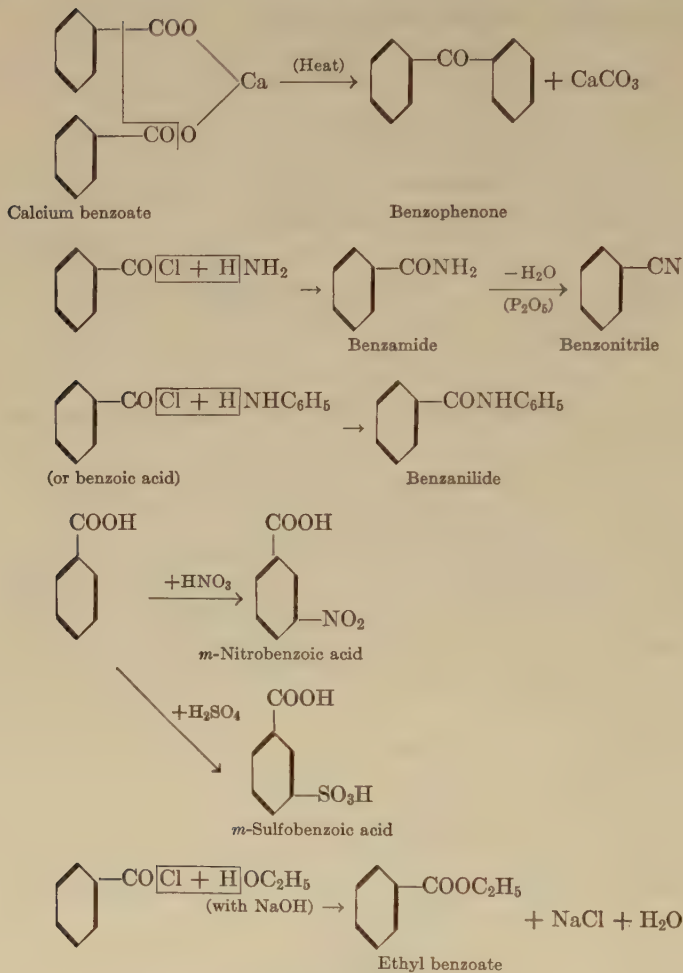
Ethyl benzoate
(used in artificial flavors
and in perfumery)



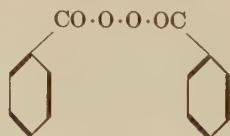
Benzoyl chloride



Benzoic anhydride



By the action of Na₂O₂ on benzoyl chloride, benzoyl peroxide,

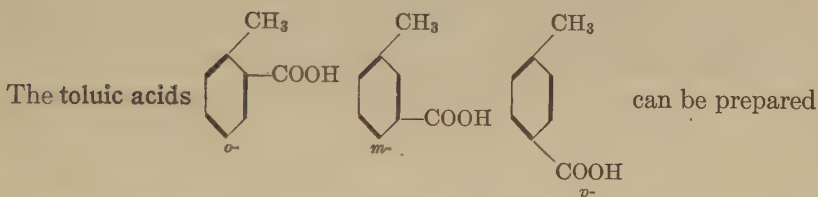
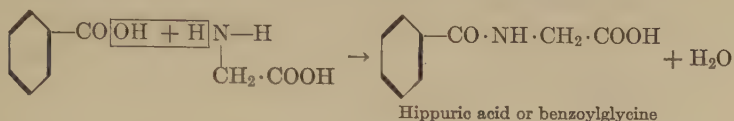


is formed. The compound is highly explosive. It is used for bleaching, for oxidation, and as a polymerization reagent.

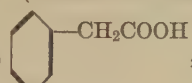
Benzoic acid itself finds application in medicine as an antiseptic and also in the manufacture of dyes. Sodium, lithium, and ammonium

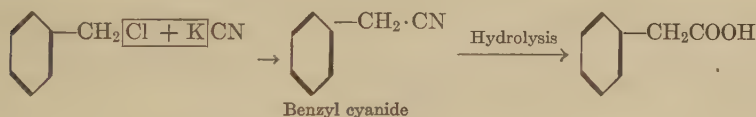
benzoates are used as internal antiseptics; sodium benzoate, as a food preservative. Benzyl benzoate is used in perfumery and as an anesthetic, and it possesses much of the pain-relieving qualities of opium without any of that drug's toxic or habit-forming dangers.

An interesting synthesis of hippuric acid in the body—by the kidneys—is brought about by the combination of benzoic acid (obtained from fruits, vegetables, and, to some extent, proteins) and the amino acid glycine (obtained from the decomposition of proteins):



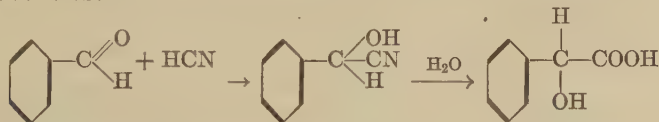
by partial oxidation of the corresponding xylenes, or from the corresponding toluidines. (Diazo and *Sandmeyer* reactions.)

Phenylacetic acid, , has its carboxyl group in the side chain and is isomeric with the toluic acids. It may be prepared from benzyl chloride:




The acid and its esters are used in perfumery.

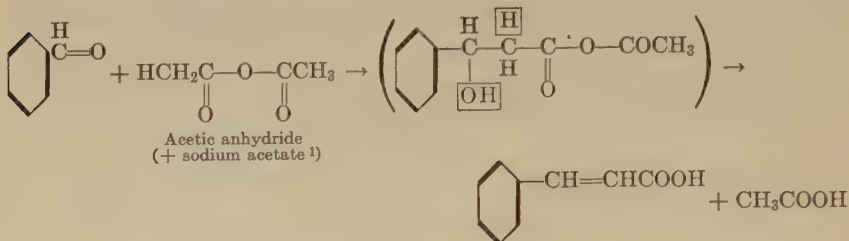
Mandelic acid, phenylglycolic acid, can be prepared from benzaldehyde as follows:



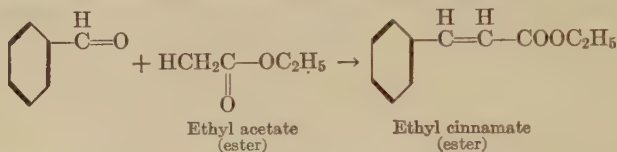
It is a bactericidal agent for the kidney.

[Note that mandelic acid has an asymmetric carbon atom. When prepared synthetically, the inactive (*dl*-) form is obtained.]


Cinnamic acid, -CH=CHCOOH, or β -phenylacrylic acid, may be prepared by *Perkin's reaction*:



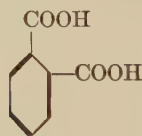
The *Perkin* condensation, which resembles the *Claisen* condensation (p. 287), is another example of aldolization. A similar *Claisen* condensation (in alkaline media) yields the corresponding ester.



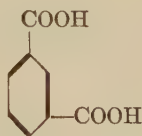
Esters of cinnamic acid and the acid itself are present in oil of cinnamon, resins, storax, balsams, gums, etc. The esters are used in flavoring materials and perfumery. The properties of cinnamic acid are those of a compound containing (a) a benzene nucleus, (b) a double-bond structure, (c) a COOH group.

Hydrocinnamic acid, -CH₂-CH₂COOH, or β -phenylpropionic acid, is prepared from cinnamic acid by reduction (sodium amalgam and water).

Of the **phthalic acids**,



Phthalic acid



Isophthalic acid

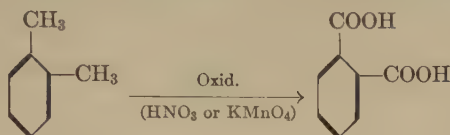


Terephthalic acid

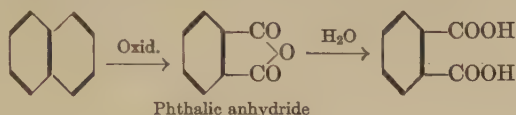
the first, phthalic acid itself, is the most important; it is used in the prep-

¹ The sodium acetate acts as a base; that is, it favors enolization and condensation. Other bases have also been used.

aration of more than 200 compounds. It may be prepared by oxidizing *o*-xylene:

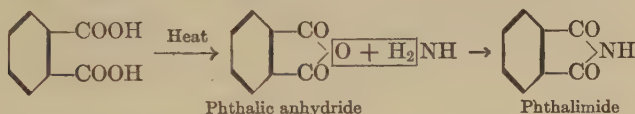


and exists mainly as the anhydride. The commercial method is to pass the vapor of naphthalene and air over vanadium pentoxide (V_2O_5) (or other catalysts) at about 400° :

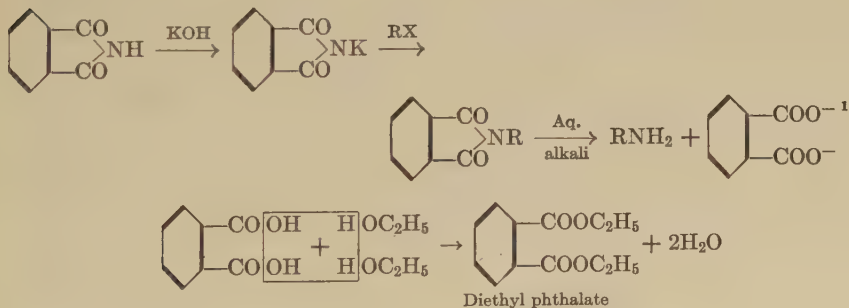


This is similar to the oxidation of benzene to maleic acid (p. 240).

Some of the reactions of phthalic acid may be summarized:



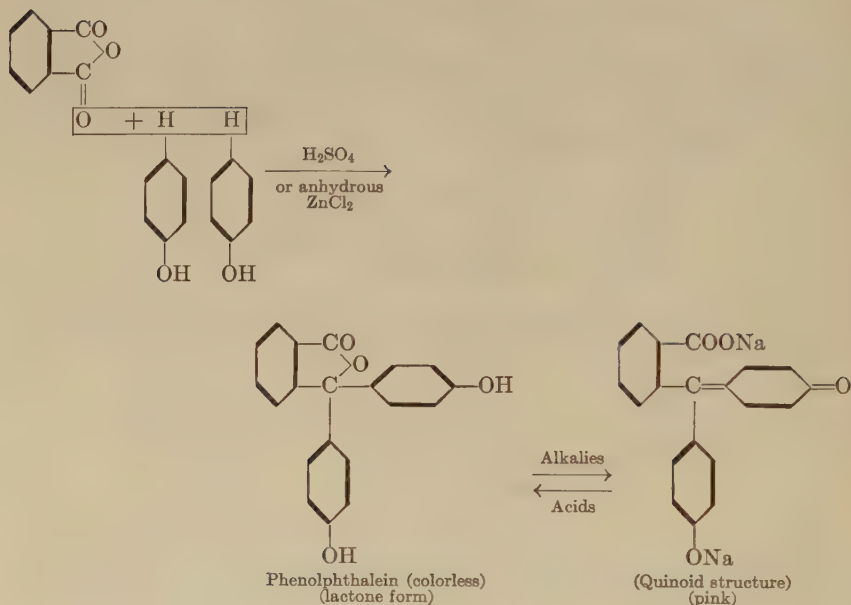
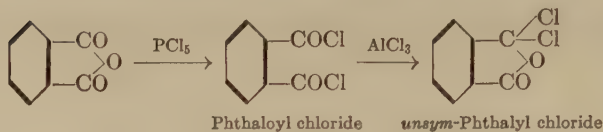
Phthalimide, like all other dibasic acid imides, possesses an active hydrogen; this makes possible the *Gabriel* synthesis of primary amines, a very useful method of making such compounds free of secondary and tertiary isomers:



Dimethyl phthalate is an efficient insect-repellent.

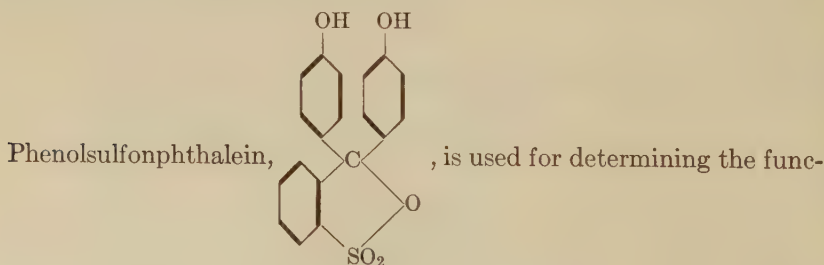
Diethyl phthalate is a bitter substance used as a denaturant for ethyl alcohol. Dibutyl phthalate (b.p. 340°C.) is used in high-vacuum distillations on account of its low vapor pressure.

¹ Compare hydrolysis of amides.



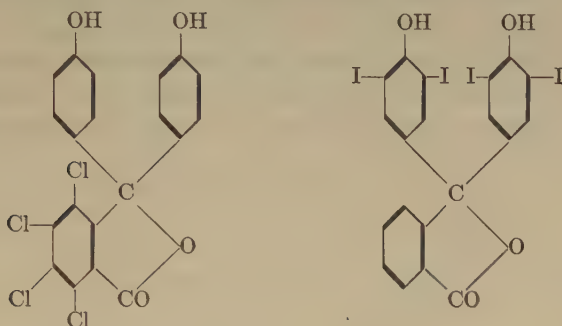
Phenolphthalein is one of the best-known indicators. It is also used as a purgative. Phthalic anhydride is utilized in the manufacture of anthraquinone (p. 330) and of several important dyes.

A considerable amount of phthalic anhydride is employed in the manufacture of synthetic resins.



Thymol blue, a common indicator, is a sulfonphthalein.

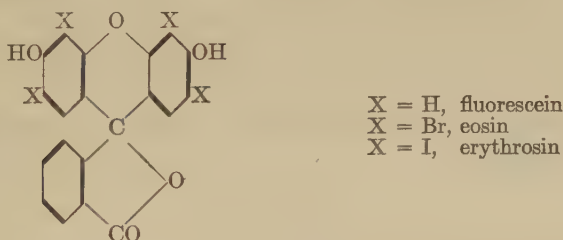
Phenoltetrachlorophthalein and tetraiodophenolphthalein,



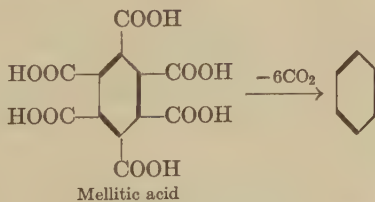
are used as indicators to test the functional activities of the liver.

Among other *phthaleins* of interest is fluorescein, a condensation product of resorcinol and phthalic anhydride, which yields a fluorescent solution in dilute alkali. In medicine, fluorescein is used to detect and diagnose foreign bodies in the cornea, etc.

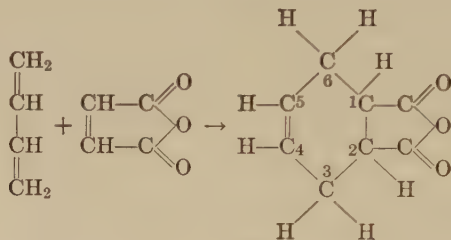
Tetrabromofluorescein, or eosin, and the tetraiodo compound, erythrosin, are of some value as dyes. Eosin is water-soluble and is a component of red inks.



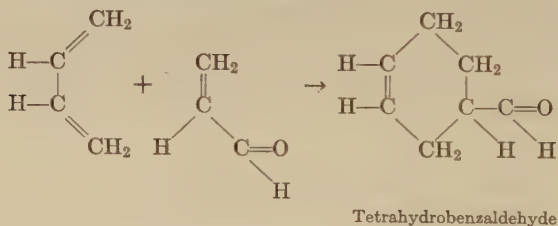
Mellitic acid, or benzene hexacarboxylic acid, may be prepared by the oxidation of graphite with HNO_3 . Its aluminum salt occurs in nature as the mineral honeystone. When heated with soda lime, the acid is converted into benzene:



The Diels-Alder Diene Synthesis. This synthesis, a valuable tool in the hands of the organic chemist, may be considered an addition between a compound containing a carbon-carbon conjugated system (a system of alternate double bonds) and one containing a carbon-carbon double bond, generally a carbonyl compound. For example, maleic anhydride combines with butadiene to form Δ^4 -tetrahydrophthalic anhydride:



Another example is the combination of butadiene with acrolein:



Alicyclic structures made in this way can be dehydrogenated to aromatic compounds.

QUESTIONS

1. Compare the methods of preparation and the general chemical properties of aliphatic and aromatic acids.
2. Outline the commercial methods of production of the following: (a) benzoic acid; (b) ethyl benzoate; (c) cinnamic acid; (d) phthalic anhydride; (e) phenolphthalein.
3. Write structural formulas for the following compounds: (a) benzoic acid; (b) cinnamic acid; (c) sodium cinnamate; (d) ethyl cinnamate; (e) phenylacetic acid; (f) phenyl acetate; (g) hydrocinnamic acid; (h) *o*-toluic acid; (i) phthalic acid; (j) terephthalic acid; (k) isophthalic acid; (l) phenolphthalein; (m) phenolsulfonphthalein; (n) tetrachlorophenolphthalein; (o) phenoltetrachlorophthalein; (p) mellitic acid; (q) benzoyl peroxide; (r) benzoic anhydride; (s) benzamide; (t) benzoyl chloride.
4. Write equations for the preparation of benzoic acid, starting with (a) benzaldehyde; (b) benzyl alcohol; (c) benzonitrile; (d) benzonitrile; (e) aniline; (f) benzene; (g) benzenesulfonic acid; (h) toluene; (i) ethylbenzene.

5. Write equations for the preparation of the following, starting with benzoic acid: (a) sodium benzoate; (b) ammonium benzoate; (c) calcium benzoate; (d) methyl benzoate; (e) benzene; (f) benzoyl chloride; (g) benzoic anhydride; (h) benzamide; (i) phenyl cyanide; (j) benzophenone; (k) benzoyl peroxide; (l) *m*-nitrobenzoic acid; (m) *m*-sulfobenzoic acid.

6. Write equations for the preparation of the following compounds:

(a) phthalic anhydride	from naphthalene
(b) hydrocinnamic acid	" benzaldehyde
(c) α,β -dibromo- β -phenylpropionic acid	" cinnamic acid
(d) phenylacetic acid	" toluene
(e) phenolphthalein	" naphthalene
(f) diethyl phthalate	" phthalic anhydride
(g) <i>m</i> -sulfobenzoic acid	" nitrobenzene
(h) benzamide	" toluene
(i) hydrobenzamide	" toluene
(j) <i>n</i> -amylamine	" naphthalene and <i>n</i> -amyl alcohol

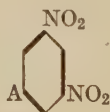
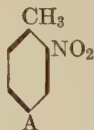
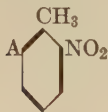
CHAPTER XXVI

ADDITIONAL AROMATIC COMPOUNDS CONTAINING MIXED GROUPS

So far we have considered largely compounds containing single groups attached to the benzene ring, such as nitro compounds, sulfonic acids, phenols, and aldehydes; and also, to some extent, a number of compounds containing dissimilar or mixed groups. In this chapter we shall consider additional compounds with unlike or mixed groups attached to the benzene ring. As thousands of such substances are known, only a few of the common and important ones can be mentioned.

Substitution in the Benzene Ring. The Introduction of a Third Substituent. We have seen how the position taken by an element or group entering the ring of a monosubstitution product may be predicted (p. 243). What about an element or group entering the ring of a disubstitution product? Even here a certain amount of prediction is still possible. The prediction is based upon a knowledge of the orienting influence of each group already present, and upon the relative strength of the orienting group. In general, the relative order of strengths is: in the *ortho*-, *para*-orienting groups, the rate of substitution decreases in the order $\text{OH} > \text{NH}_2 > \text{Cl} > \text{I} > \text{Br} > \text{CH}_3$; in the *meta*-orienting groups, the rate of substitution varies in the order $\text{COOH} > \text{SO}_3\text{H} > \text{NO}_2$. In addition it may be said that the rate of *ortho*-, *para*-substitution is much greater than that of *meta*-substitution.

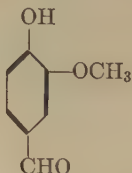
Using A as the third entering substituent, the following examples may be given:



However, it must be emphasized that other isomers are also formed simultaneously, depending upon experimental conditions.

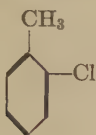
[Note: In studying the following compounds, the student should bear in mind that each group attached to the ring is responsible for certain characteristic reactions, and that the properties of the compound as a

whole are, as a rule, the summation of properties exhibited by the individual groups present. For example, such a compound as

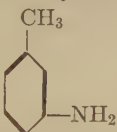


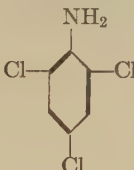
has properties due (a) to the benzene ring, (b) to the OH group, (c) to the OCH₃ group, and (d) to the CHO group.]

Chlorotoluenes, or tolyl chlorides. Three isomers are known:

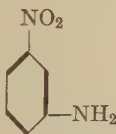
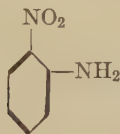


A mixture of the first two (*o*- and *p*-) is obtained when toluene is chlorinated (in the presence of a halogen carrier). Direct chlorination of toluene does not yield the third, or *m*-, variety; but we may start with

m-toluidine, , diazotize it, and apply the *Sandmeyer* reaction.

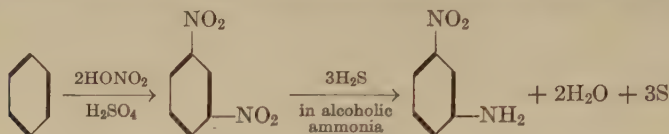
Three isomeric **chloroanilines** are known. When aniline is treated with chlorine, *sym*-trichloroaniline, , is obtained.

Of the three **nitroanilines**

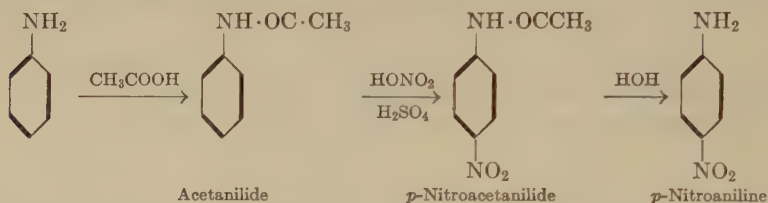


the second (*m*-variety) is prepared by treating benzene with nitric and sulfuric acids to produce the *m*-dinitrobenzene, and then employing a

sufficiently mild reducing agent to reduce but one of the NO_2 groups:

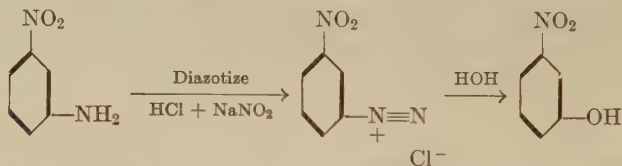


The *p*-nitroaniline is obtained as follows:

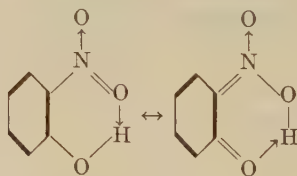


The object of first acetylating is to "muzzle" the NH_2 group (p. 266); in other words, the NH_2 group must be protected against the oxidizing action of nitric acid.

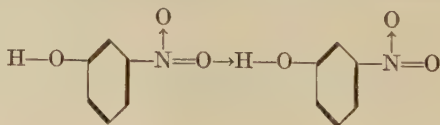
The *o*- and *p*-**nitrophenols** are prepared by direct nitration of phenol; the *m*- variety is prepared from *m*-nitroaniline:



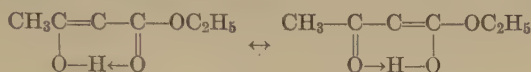
o-Nitrophenol differs from its isomers in being readily volatile with steam, much lower in boiling point, and more soluble in benzene. This has been explained by the existence of a ring structure in the *ortho* isomer, a *chelate* structure with a hydrogen bond



which cannot exist for *m* and *p* compounds. These two can, therefore, form intermolecular *association* compounds which would be more polar in behavior, since some functional groups would be free to react as usual:

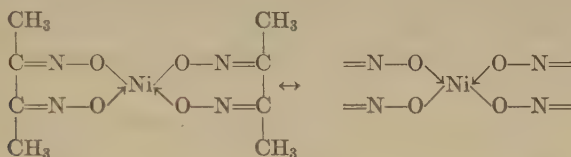


Infra-red spectra have confirmed the possibility of chelation, which, as indicated, involves resonance and can be used to explain the existence of stable compounds where they might not be expected, as in the case of the enol form of acetoacetic ester:

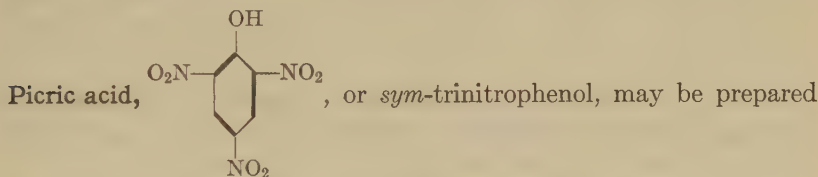


This may serve to account for the unusual stability of the enol structure, which, as we may remember, itself contributes to a resonating keto-enol system.

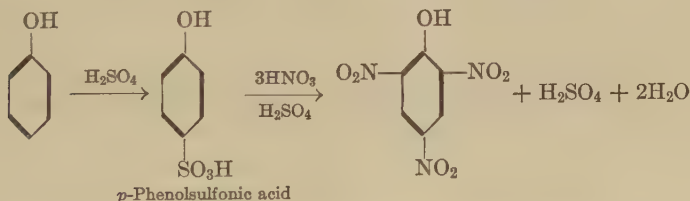
The metallic salts of organic compounds like dimethylglyoxime,



are best represented as chelate ring compounds: they are non-polar, form no ions, and dissolve more readily in organic solvents than in water. Some complex inorganic molecules behave similarly and are assigned similar structures.



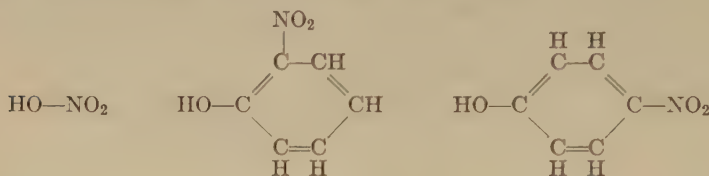
from phenol by nitration. Commercially, it is manufactured thus:



Picric acid is a strong acid, the increased acidity being due to the presence of nitro groups. Even the mononitro- and dinitrophenols are stronger acids than phenol, some of them acting as indicators.

An interesting connection between structure and properties can be shown in such cases as these. If we examine the structures of nitric

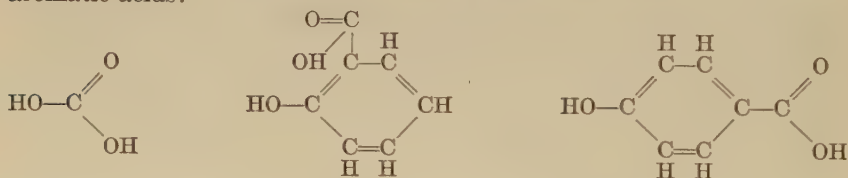
acid and of the *o*- and *p*-nitrophenols, for instance,



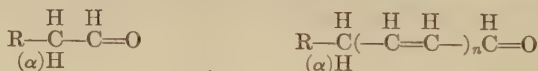
we see that the $\text{HO}-\text{NO}_2$ differs from the other two in the fact that the grouping $(-\text{CH}=\text{CH}-)_n$ separates the two functional groups, the three compounds, as well as the polynitrophenols, being rather strong acids.

The transmission of chemical influence through the "vinylene" groups has been designated as *vinylology* by *Fuson* and has been helpful in pointing out many similarities of behavior in compounds of apparently diverse structure.

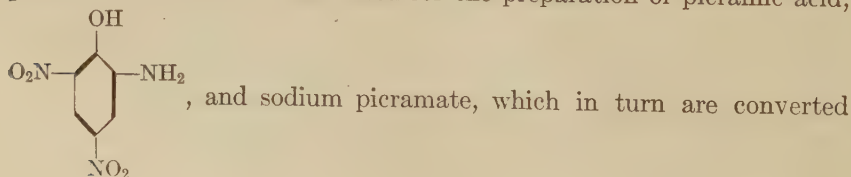
To take another example, the *o*- and *p*-hydroxybenzoic acids, vinyllogs of carbonic acid, lose CO_2 on heating much more readily than other aromatic acids:




Similarly, in respect to α,β -unsaturated carbonyl compounds and their homologs with conjugated double bonds, the influence of $\text{C}=\text{O}$ on the α -carbon is transmitted through the vinylene groups:




Picric acid is used in a colorimetric method for determining glucose in the blood, as a test for creatinine, as a precipitant for organic bases and proteins, as a "fixing" agent in histological work, in the treatment of skin diseases and of burns, as an antiseptic, and in the manufacture of explosives. Picric acid is also used for the preparation of picramic acid,



into several green and brown dyes. Many of the nitro compounds of the aromatic series, such as picric acid and TNT, are powerful explosives.

Sulfanilic acid, , *p*-aminobenzenesulfonic acid, is prepared from

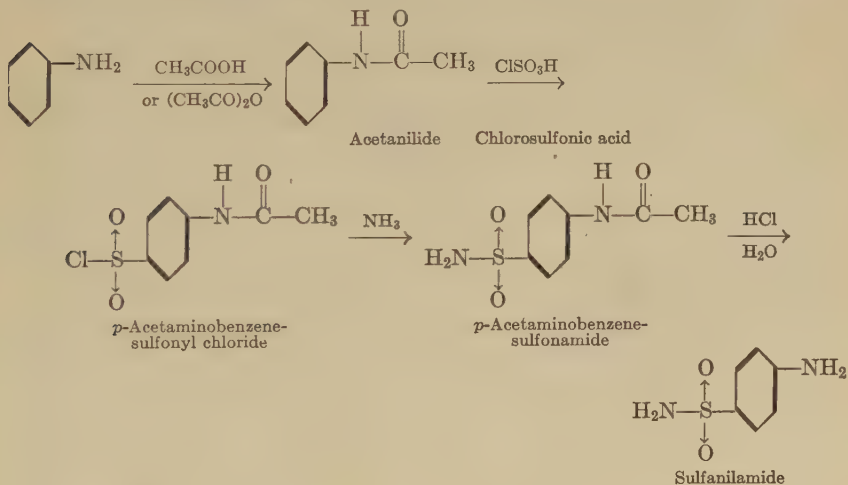
aniline by treatment with concentrated sulfuric acid, which first forms

aniline acid sulfate, ; this on heating at 180° for several

hours is converted to sulfanilic acid. The acid is used in the manufacture of several dyes. Since this compound contains a basic —NH₂— and an acidic —SO₃H— group, it can be written as a dipolar ion:



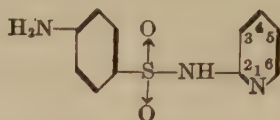
Sulfanilamide, *p*-aminobenzenesulfonamide, is prepared from aniline by the following series of reactions:



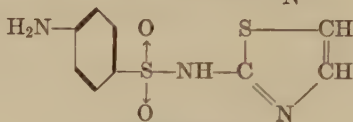
Sulfanilamide and a number of its derivatives have come into extensive use in treating hemolytic and pneumococcic infections. It is probable that, since *Ehrlich's* discovery of salvarsan, no compound for medicinal purposes has been so widely used.

A number of derivatives which have been useful are:

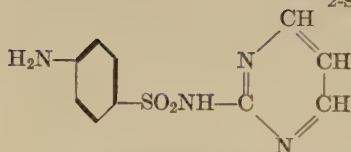
Sulfapyridine, 2-sulfanilylaminopyridine,



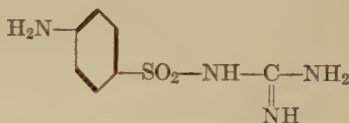
In structure, it may be regarded as sulfanilamide in which the H of the sulfonamide group is replaced by pyridine,



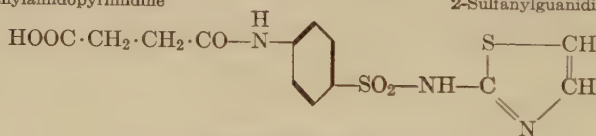
Sulfathiazole
2-Sulfanilylamidothiazole



Sulfadiazine
2-Sulfanilylamidopyrimidine



Sulfaguanidine
2-Sulfanilylguanidine

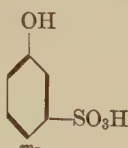
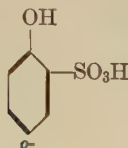


Succinylsulfathiazole
2-(p-succinylaminobenzenesulfonamido)thiazole¹



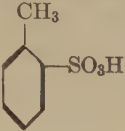
is **metanilic acid**. It is prepared by reducing *m*-nitrobenzenesulfonic acid, and is used in the preparation of azo dyes.

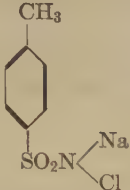
Of the **phenolsulfonic acids**,




¹ A substance, **penicillin**, obtained from a mold, *Penicillium notatum*, is being used with great success in the war against bacterial infections. It is *bacteriostatic* in its action—it inhibits the growth and multiplication of various types of pathogenic bacteria—and (this is its great advantage) it is not toxic to the body.

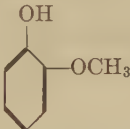
the *o*-variety is prepared by treating phenol with H_2SO_4 (in the cold); the *p*-, by heating phenol with H_2SO_4 to 96° ; and the *m*-, by cautiously fusing (with NaOH) the *m*-benzenedisulfonic acid. A mixture of the *o*- and *p*- is used as an antiseptic under the name 'Aseptol.'

***o*-Toluenesulfonic acid**, , is used in the preparation of saccharin (p. 318).

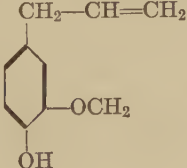
Chloramine-T, , sodium-*p*-toluenesulfon-N-chloramide, or

"chlorazene" (a derivative of *p*-toluenesulfonic acid), is used as an irrigating fluid in the treatment of wounds, as a mouth wash, and, in general, as an active germicide. It has approximately four times the antiseptic value of phenol. It was introduced by *Carrel* and *Dakin* during World War I.

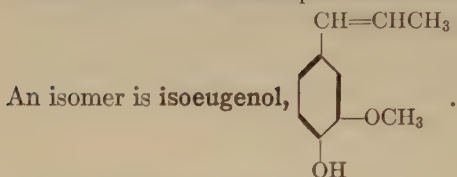
Dichloramine-T, , or *p*-toluenesulfon-N-dichloramide, is also used in the treatment of infected wounds.

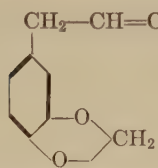
Guaiacol, , *o*-methoxyphenol, the monomethyl ether of


catechol, is found in gum guaiacum and in beechwood tar, and is obtained from guaiac resin by distillation. The guaiac resin, dissolved in alcohol, is the "guaiac reagent" used in tests for oxidizing enzymes, blood, milk, etc. Guaiacol, as well as some of its salts and esters, is used as an internal antiseptic.


Eugenol, , 4-allyl-2-methoxyphenol, is present in oil of

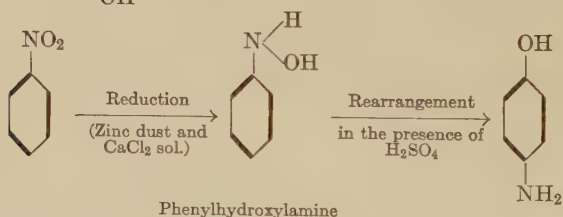
cloves. It is an antiseptic and local anesthetic used in dentistry.



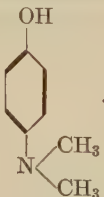
Safrole, , 1-allyl-3,4-methylenedioxybenzene, is the chief constituent of oil of sassafras. It is used as an anodyne.

Anethole, , *p*-propenylanisole, is found in anise-seed oil and is used as an antiseptic.

***p*-Aminophenol**, , is prepared as follows:

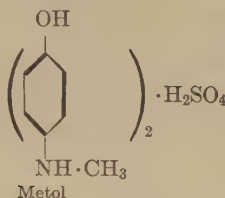
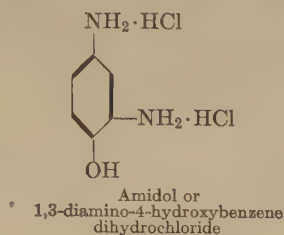
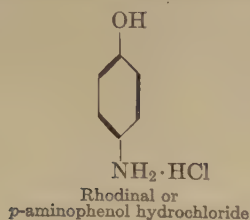


or by the reduction of *p*-nitrophenol, and is used as a photographic developer and in the manufacture of such dye intermediates as *p*-hydroxy-

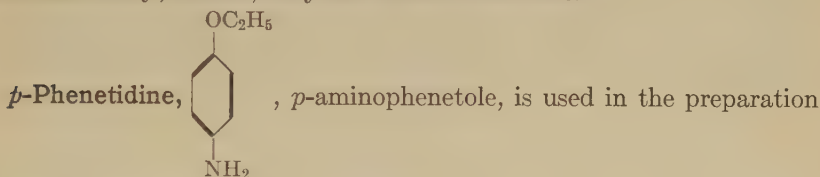
dimethylaniline, . The 1,4 or *p*-aminophenol type of compound

and its derivatives make the best photographic developers, that is, reducing agents appropriate for the reactions involved ($\text{Ag}^+ \rightarrow \text{Ag}^\circ$).

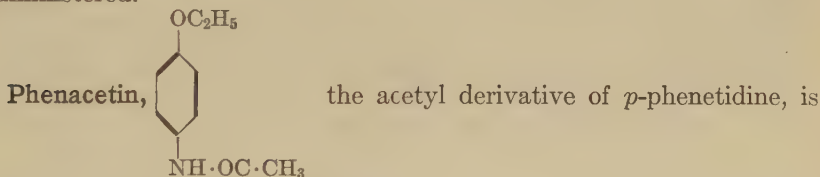
Some of the compounds used as photographic developers are:



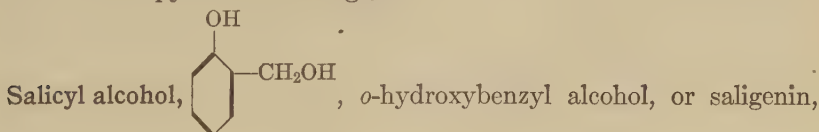
Most developers have OH and/or NH₂ groups in *p*-positions. All phenols and amines oxidize readily (fresh samples become colored quickly), but the diphenols, diamines, and aminophenols are oxidized more smoothly; that is, they are effective reducers.



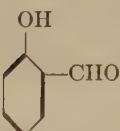
of phenacetin, and it often appears in the urine when phenacetin is administered.

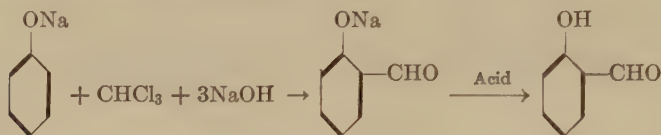


used as an antipyretic and analgesic.

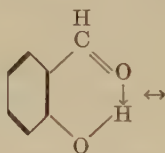


occurs in combination with glucose in the glucoside salicin (present in willow bark). It has been assumed to be the first product in the formation of phenol-formaldehyde polymers. It has been recommended as a local anesthetic.

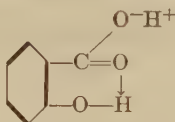
Salicylaldehyde, , *o*-hydroxybenzaldehyde, is prepared by the *Reimer-Tiemann* reaction:



The *p*-modification is also produced, but the *o*- and *p*- can be separated by steam distillation, the *o*- passing over with the steam. Here again the possibility of a chelate structure (p. 306) serves to account for the marked difference in behavior:




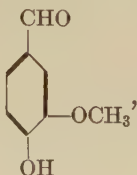
A similar explanation has also been given to correlate the structure with the noticeably greater acidity of *o*-substituted benzoic acids such as salicylic:



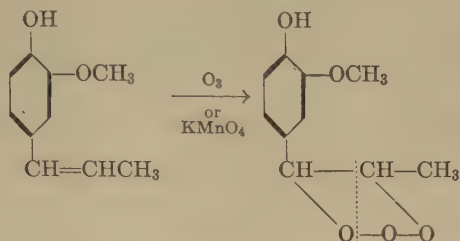
Chelation absorbs part of the attraction of the carboxylate ion for the proton and thus allows for a higher concentration of protons.

Salicylaldehyde occurs in oil of spiraea and oils of certain flowers and is used in perfumery and in the preparation of coumarin (p. 340).

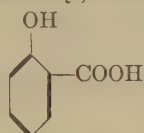
Anisaldehyde, , or *p*-methoxybenzaldehyde, is found in anise-seed oil and is used in perfumery.

Vanillin, , *m*-methoxy-*p*-hydroxybenzaldehyde, is present

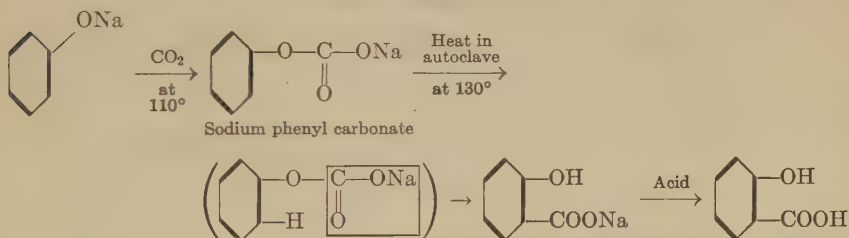
in vanilla bean and is the chief constituent of extract of vanilla. It is manufactured by the oxidation of isoeugenol:



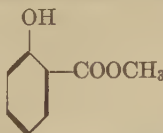
and also from guaiacol by the *Reimer-Tiemann* reaction (see p. 314). It is used in perfumery, as a flavoring agent, and as a gastric stimulant.

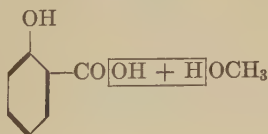
Salicylic acid, , *o*-hydroxybenzoic acid, occurs in blossoms

of meadow sweet, and as its methyl ester in oil of wintergreen. It is prepared by the *Kolbe-Schmitt* reaction:

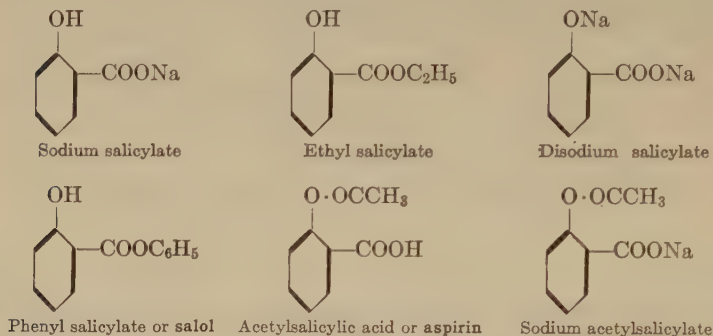


Salicylic acid is commonly administered in the form of some of its derivatives, such as salol, aspirin, sodium salicylate, and methyl salicylate. Large quantities are used in the manufacture of dyestuffs.

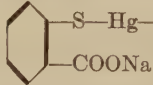
Methyl salicylate, , is the chief constituent of oil of wintergreen and oil of sweet birch; it is the artificial oil of wintergreen. It is prepared by heating salicylic acid with methanol:



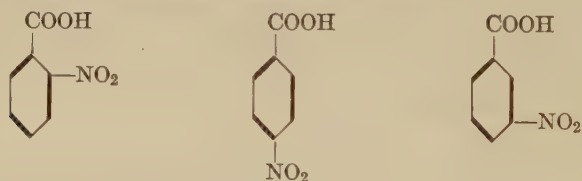
A number of the salicylates and their derivatives, such as



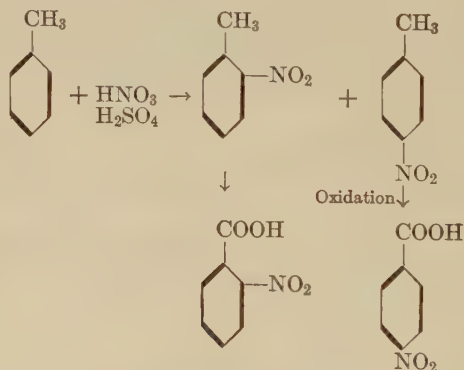
are used as intestinal antiseptics and as antipyretics.

Merthiolate, , a mercury-sulfur derivative of salicylic acid, is used as a germicide for disinfecting tissue surfaces and instruments. It is much less toxic than mercuric chloride.

There are three isomers of **nitrobenzoic acid**,





the first two being prepared from toluene:

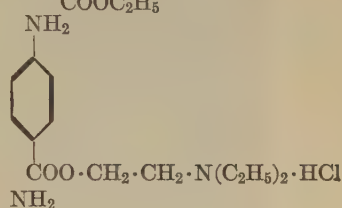


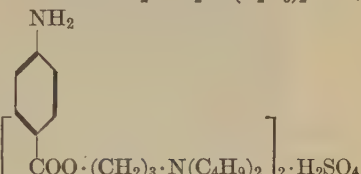
and the *m*-variety, by direct nitration of benzoic acid. On reduction they yield the corresponding amino acids.

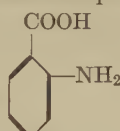
***p*-Aminobenzoic acid** is considered to be a member of the vitamin B complex (p. 393).

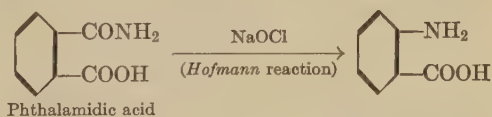
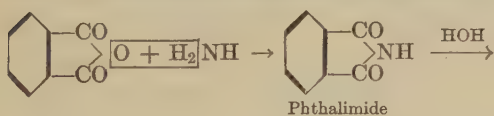
A number of derivatives of *p*-aminobenzoic acid, , are important

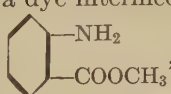
local anesthetics. Anesthesine or benzocaine is , ethyl *p*-amino-

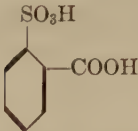
benzoate. **Novocaine** or procaine is 

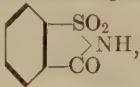
It is less toxic than cocaine. Butyn,  is used in dentistry and in ophthalmic surgery.

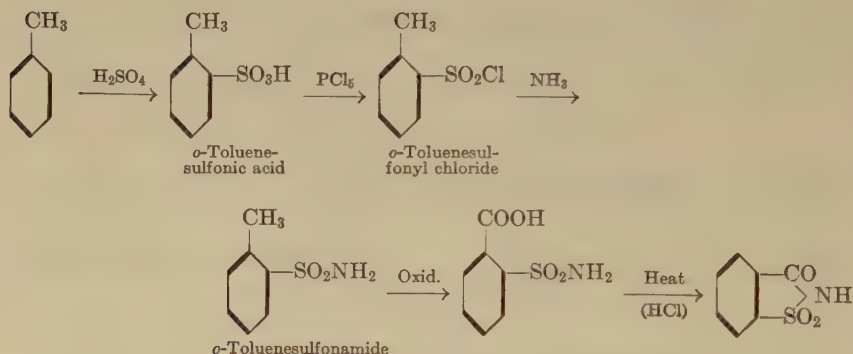
Anthranilic acid, , *o*-aminobenzoic acid, is prepared either from *o*-nitrobenzoic acid by reduction, or from phthalic anhydride:




It is used as a dye intermediate and in the synthesis of esters. Methyl anthranilate, , a constituent of orange blossoms, is used in flavors (grape) and in perfumery.

***o*-Sulfobenzoic acid**, , is prepared by the sulfonation of toluene and the subsequent oxidation of the CH₃ group.

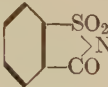
Saccharin, , *o*-benzoic sulfimide, may be prepared as follows:



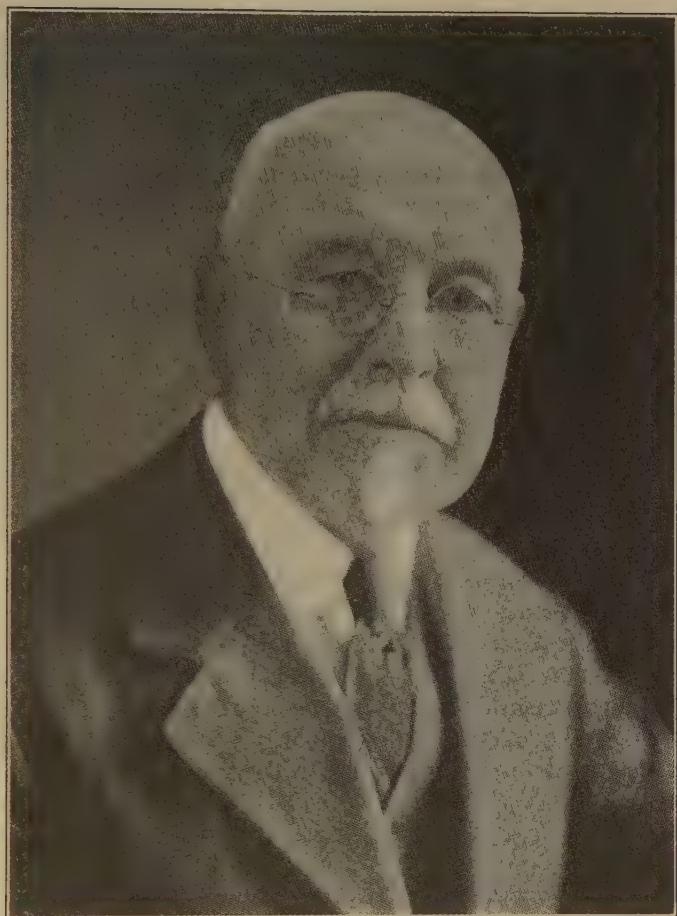
When toluene is sulfonated a mixture of *o*- and *p*-compounds is, of course, formed. They are separated at the sulfonyl chloride stage,

, by filtering them with ice; the *p*-compound, being a solid at that temperature, remains on the filter, the *o*-going through in the form of a thick, oily liquid.

Saccharin was first prepared by *Remsen*. It is said to be about 550 times as sweet as sugar, and it is used as a substitute for sugar by diabetics, and as a sweetening agent in mouth washes, tooth pastes, etc. The substance has no nutritive value. Since saccharin itself is not very

soluble in water, the sodium salt , which is very soluble, is manufactured.

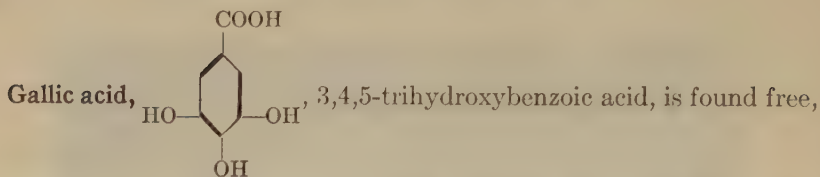
p-Toluenesulfonyl chloride is employed with *p*-toluenesulfonamide as a camphor substitute. *p*-Toluenesulfonic acid is also used in the manufacture of dyes. *p*-Toluenesulfonamide is employed in the preparation of chloramine-T.



Ira Remsen.

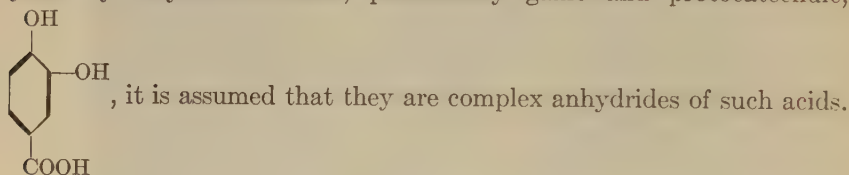
IRA REMSEN (1846-1927)

For many years professor of organic chemistry at Johns Hopkins University (and later its president), is best known for his work on saccharin (p. 318) and as the author of textbooks on organic chemistry. He did much to further research in organic chemistry in this country.



or as a glucoside in a number of plants (sumach, gall nuts, etc.), and may also be obtained by hydrolyzing tannins with acid. When it is heated, CO_2 is evolved and pyrogallol is formed. Gallic acid is used in photography, in inks, and as an astringent.

Tannic acids. These acids are found in gall nuts and other plants. Their exact constitution is not known, but since, on hydrolysis, they yield hydroxybenzoic acids, particularly gallic and protocatechuic,



The mother substances of these tannic acids are tannins, which are glucosides. The names "tannic acid" and "tannins" are commonly used interchangeably. These tannins are found in gall nuts, oak, chestnut, pine, hemlock, etc. They give characteristic blue-black or green-black colors with ferric chloride and are valuable astringents. They precipitate proteins and alkaloids. They are largely employed in the making of leather, as mordants in dyeing, and in the manufacture of inks.

QUESTIONS

- Write structural formulas for (a) pyrogallol; (b) anthranilic acid; (c) saccharin; (d) vanillin; (e) picric acid; (f) *p*-nitroaniline; (g) acetanilide; (h) *o*-tolyl chloride; (i) sulfanilic acid; (j) metanilic acid; (k) chloramine-T; (l) guaiacol; (m) eugenol; (n) aspirin; (o) salicylic acid; (p) salicylaldehyde; (q) methyl salicylate; (r) methyl anthranilate; (s) *o*-sulfobenzoic acid; (t) gallic acid; (u) phenetidine; (v) salicyl alcohol; (w) phenacetin; (x) sodium phenyl carbonate; (y) sulfanilamide; (z) sulfapyridine.
- Write equations for the preparation of the following compounds:

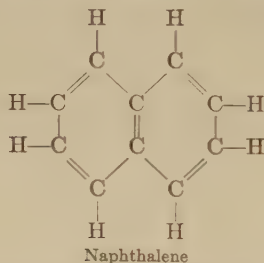
(a) picric acid	from benzene
(b) sulfanilic acid	" benzene
(c) metanilic acid	" benzene
(d) phenacetin	" benzene
(e) salicylaldehyde	" benzene
(f) vanillin	" benzene
(g) aspirin	" benzene
(h) saccharin	" benzene

(i) <i>p</i> -aminophenol	"	nitrobenzene
(j) anthranilic acid	"	naphthalene
(k) phenylacetic acid	"	toluene
(l) pyrogallol	"	gallic acid
(m) <i>p</i> -nitroaniline	"	benzene
(n) sulfanilamide	"	benzene
(o) <i>m</i> -nitroaniline	"	benzene

CHAPTER XXVII

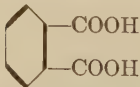
NAPHTHALENE, ANTHRACENE, AND THEIR DERIVATIVES

So far we have considered aromatic compounds containing the benzene nucleus; now we shall discuss compounds containing two or more condensed benzene rings, in which two carbon atoms are common to both rings:




Naphthalene and anthracene are the most important of such compounds.

Naphthalene. This hydrocarbon is obtained from coal tar in the fraction distilling over between 170° and 230° (middle or carbolic oil fraction). (See chart facing p. 236.) The crude product so obtained is purified by sublimation. Naphthalene crystallizes in lustrous plates, having a melting point of 80° and a boiling point of 218° . It is very volatile and has a characteristic odor. It is used in the preparation of naphthalene derivatives, in mothballs, as an insecticide and germicide, and in the manufacture of phthalic anhydride and dye intermediates.

Naphthalene has the formula $C_{10}H_8$ and on oxidation yields phthalic acid, , which proves the hydrocarbon to contain a benzene

ring, as well as two side chains in the *o*-position with respect to each other. That the actual constitution of naphthalene corresponding to

$C_{10}H_8$ is , or two condensed benzene rings, is suggested by a

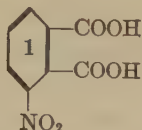
number of reactions, of which two will be mentioned.

Naphthalene, like benzene, can be readily nitrated, yielding nitro-naphthalene, which is reduced to aminonaphthalene. When nitro-

naphthalene is oxidized, we get nitrophthalic acid; when aminonaphthalene is oxidized, we do not get aminophthalic acid, but just phthalic acid. If we write the structure for nitronaphthalene as



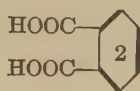
then it is plain that, on oxidation, ring 2 must be oxidized to yield nitrophthalic acid



whereas if we write aminonaphthalene as



then it is equally evident that ring 1 must here be oxidized to yield phthalic acid

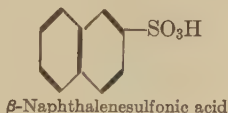
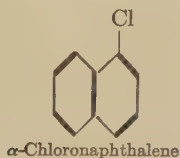


Obviously, then, there must be two benzene rings in naphthalene—two benzene rings having two carbon atoms in common.

Naphthalene has 8 replaceable hydrogen atoms:

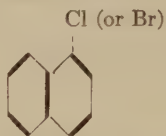


Since the molecule is symmetrical in structure, positions 1, 4, 5, and 8 are identical, and positions 2, 3, 6, and 7 are identical. We therefore have two possible monosubstitution products, a substituent at position 1 (or 4, 5, 8) being known as α - (*alpha*), and a substituent at position 2 (or 3, 6, 7) being known as β - (*beta*). For example,

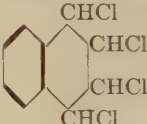


With disubstitution products, where the substituents are the same, 10 isomers are possible: 1 : 2, 1 : 3, 1 : 4, 1 : 5, 1 : 6, 1 : 7, 1 : 8, 2 : 3, 2 : 6, 2 : 7; but where they are dissimilar, 14 isomers become possible. Many substitution products and derivatives of naphthalene are manufactured, since they are used as dye intermediates, but only a few will be discussed here.

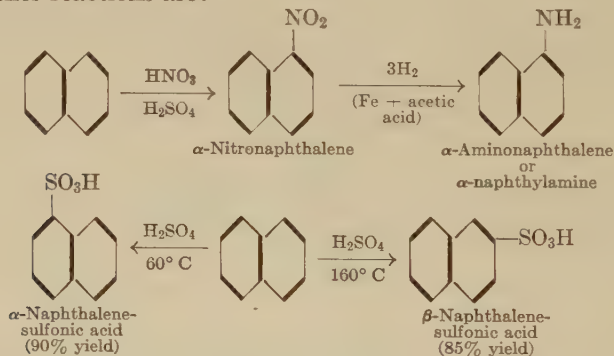
α -Chloro (or bromo) naphthalene



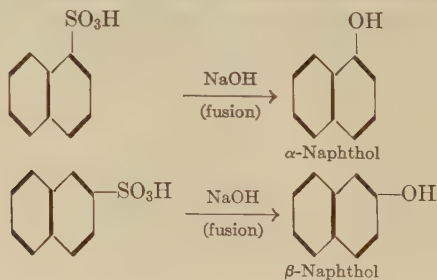
is prepared by the direct action of chlorine (or bromine) on boiling naphthalene. The β -chloro- or bromo-naphthalene is prepared by indirect methods, such as, for instance, a *Sandmeyer* reaction with diazotized β -aminonaphthalene. On the other hand, when chlorine (from potassium chlorate and HCl) is allowed to act on the hydrocarbon,

naphthalene tetrachloride, , an addition product, is obtained.

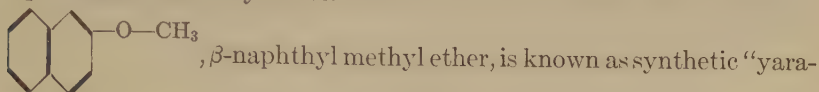
Some other reactions are:



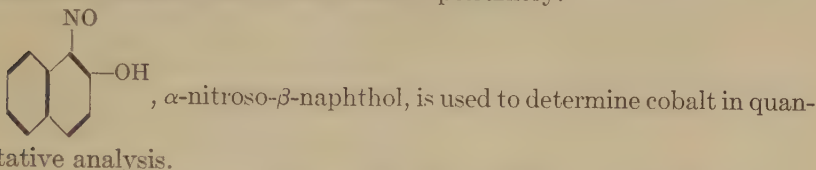
The sulfonic acids are used in the manufacture of naphthols:



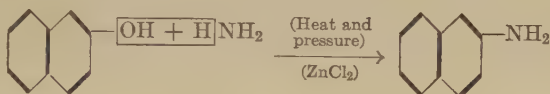
These reactions, it will be noticed, are entirely analogous to the preparation of phenol from benzenesulfonic acid. The naphthols are very important dye intermediates. α -Naphthol is also used to test for the presence of carbohydrates.



yara" and is used in perfumery. The β -naphthyl ethyl ether is known as synthetic "nerolin" and is also used in perfumery.



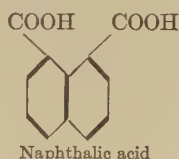
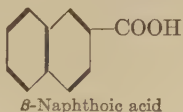
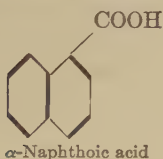
α -Naphthylamine is prepared from naphthalene (p. 322), and β -naphthylamine from β -naphthol:



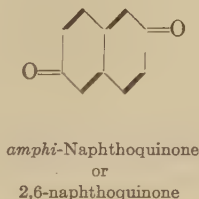
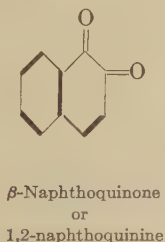
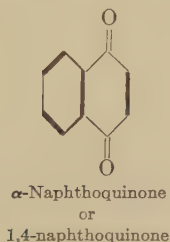
α -Naphthylamine can be made similarly from α -naphthol.

The β -naphthylamine may also be obtained by heating β -naphthol with ammonium chloride and NaOH in an autoclave at 160° . The naphthylamines are used extensively for the manufacture of dye intermediates and azo dyes (p. 351). Just as the NH_2 group in aniline, etc., can be diazotized, so can the NH_2 group in naphthalene compounds.

Examples of acids derived from naphthalene are:

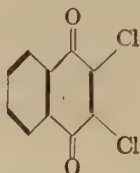


Naphthalene forms three quinones:

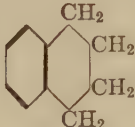


The α -quinone may be prepared by oxidizing naphthalene with chromic acid in the presence of glacial acetic acid. This 1,4-naphthoquinone is an essential part of the structure of vitamin K (p. 398).

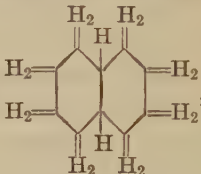
Among the dichloro isomers, 2,3-dichloro-1,4-naphthoquinone



is a potent fungicide.

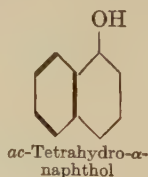
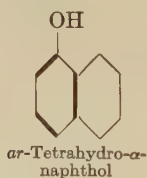
"**Tetralin**," or tetrahydronaphthalene, , which has been

suggested as a motor fuel and solvent, is prepared by reducing naphthalene with hydrogen in the presence of nickel as catalyst. A somewhat

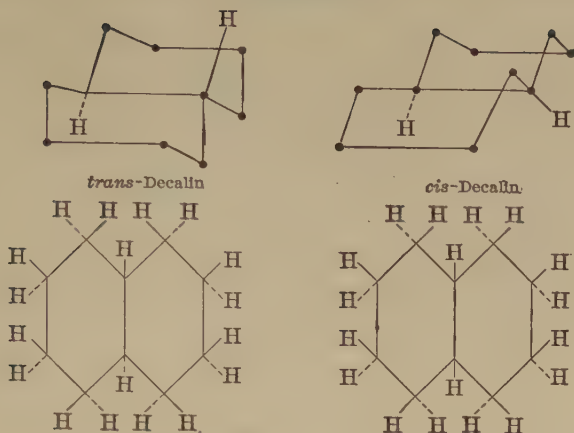
similar compound, "**decalin**," or decahydronaphthalene, ,

has also been suggested as motor fuel and solvent. These two compounds are also used in textile soaps and in detergents.

Tetralin, decalin, and their derivatives are alicyclic compounds. Tetralin forms two series of derivatives, one being the so-called aromatic (*ar*) derivatives, in which the functional group is in the aromatic or unhydrogenated ring; in the other or alicyclic (*ac*) series, functional group and hydrogens are in the same ring and show aliphatic behavior:



Decalin may be considered a fusion of two cyclohexane rings, and, from that point of view, the actual existence of two decalins is explained rather easily:



With the exception of the "angular" C atoms,¹ each carbon atom has one hydrogen above and one below the plane of the carbon ring.

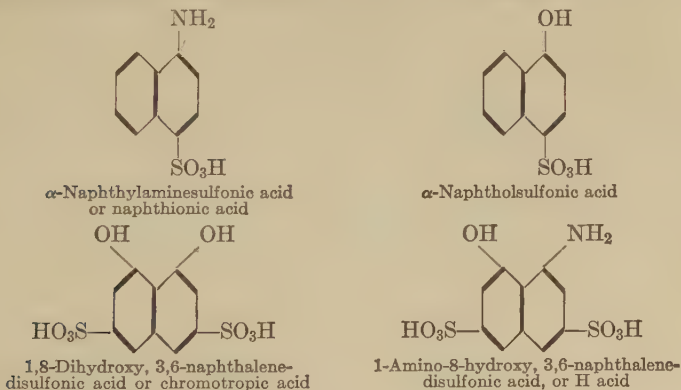
As a matter of fact, four β -monosubstituted decalins are known in which OH or NH_2 is the substituent. Their structures can be written as derivatives of the two stereoisomeric decalins:



In asymmetric molecules of this type, optical isomerism also may occur.

Stereoisomerism of this type is found in important groups of naturally occurring substances such as sterols (p. 397) and some hormones (p. 400), which are hydrogenated phenanthrene derivatives.

Many dye intermediates containing different substituents in the naphthalene ring are manufactured. A few of these are:

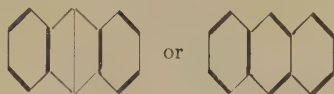


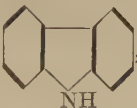
¹ An angular carbon atom is one common to two rings.

The following chart shows the position of entering substituents in the naphthalene ring.
If a hydrogen atom in naphthalene is replaced

by	Cl	Br	OH	OR	NO ₂	NH ₂	NHR	SO ₃ H	CN	COOH
in the position	1	2	1	2	1	2	1	2	1	2
the new group enters in the position										
Cl	4	4	2?	1			1		5	5
Br	4 5 or 8	4 5	1		5 or 8		4	5	5	5
NO ₂	4	4	2	1	5 6 or 7 8	5 8	2 4	4 5 8	5 ?	5 8
SO ₃ H under 100°	4 5	4 ?	2 4	6 8	5 6 7	4 5 8		5 6	5 ?	α β β
SO ₃ H above 100°	5	6	2	6 7		6 7		5 6 7		
NO			2 4	1						
COOH			2	1 3						

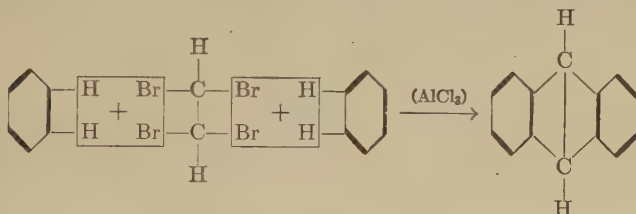
Anthracene, $C_{14}H_{10}$, or



is present in coal tar in the fraction which boils over 270° (see chart facing p. 236). From this fraction **carbazole**, , and **phenanthrene** (p. 330), are also recovered.

Anthracene (m.p. 216° , b.p. 360°) crystallizes out in the form of colorless, glistening leaflets having a blue fluorescence.

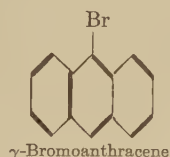
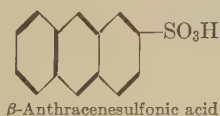
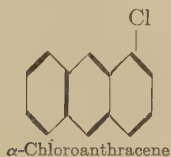
The structure of anthracene has been confirmed by a number of syntheses of the compound, one of which will be given: in the presence of $AlCl_3$, two molecules of benzene combine with one molecule of tetrabromoethane to form anthracene (*Friedel-Crafts reaction*).



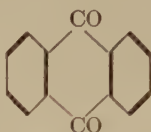
The positions of the replaceable hydrogen atoms are numbered thus:



and from this structure it may be seen that positions 1, 4, 5, and 8 bear exactly the same relationship to the molecule. This is also true of positions 2, 3, 6, and 7, and of 9 and 10. There are possible, therefore, three monosubstitution products, 1, 4, 5, or 8 being known as α -; 2, 3, 6, or 7, as β -; and 9 or 10 as γ - (gamma) or *meso*:



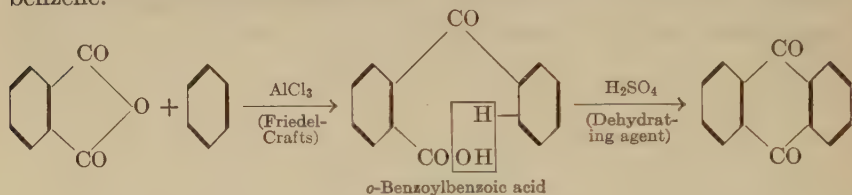
The most important derivative of anthracene is anthraquinone,



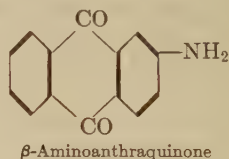
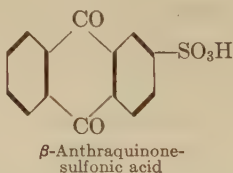
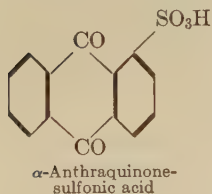
which may be prepared from anthracene by oxidation with chromic acid ($\text{Na}_2\text{Cr}_2\text{O}_7$ and H_2SO_4).

Nitric acid does not give rise to nitro derivatives with anthracene, but converts it to anthraquinone—an indication that the central nucleus in anthracene is somewhat different from the two outer benzene nuclei.

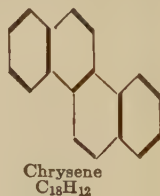
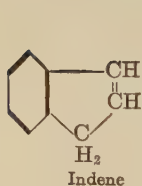
Anthraquinone is manufactured on a large scale, for it is used in the manufacture of dyes (such as alizarin, p. 356) and dye intermediates. It is produced synthetically by condensing phthalic anhydride with benzene.



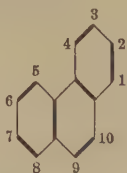
A number of other important anthraquinone derivatives used in the manufacture of dyes are:



A few other condensed ring compounds obtained from coal tar are:



Phenanthrene is also written thus:



Indene polymerizes into indene resins which are used in paints and varnishes.

The **phenanthrene** ring is found in a number of compounds of physiological importance, such as the sex hormones (p. 400), bile acids, sterols (cholesterol, ergosterol, etc., p. 396), and in cancer-producing substances (p. 401).

A careful survey of the compounds so far studied will reveal that they have been prepared by making use of one or more of the following type reactions: halogenation, reduction, alkylation, oxidation, condensation, nitration, sulfonation, amidation, alkali fusion, nitrosation, hydrolysis, internal rearrangement, etc. Many of the substances prepared in this way are classed as dye "intermediates" and are used in the preparation of dyes, which are taken up in Chapter XXX.

QUESTIONS

- Write structural formulas for (a) naphthalene; (b) anthracene; (c) phenanthrene; (d) α -naphthol; (e) β -naphthylamine; (f) α -naphthoic acid; (g) β -naphthyl ethyl ether; (h) α -naphthyl benzoate; (i) tetralin; (j) decalin; (k) α -naphthoquinone; (l) β -naphthoquinone; (m) anthraquinone; (n) *o*-benzoylbenzoic acid; (o) benzyl α -naphthoate; (p) benzyl benzoate; (q) benzoic anhydride; (r) α -aminoanthraquinone; (s) β -chloroanthraquinone; (t) α -hydroxyanthraquinone; (u) 1,7-dihydroxy-3,6-naphthalenedisulfonic acid; (v) α -nitroso- β -naphthol; (w) naphthionic acid; (x) γ -bromoanthracene; (y) *amphi*-naphthoquinone; (z) 1-amino-2-hydroxy-6,8-disulfo-9,10-anthraquinone.

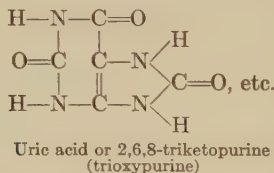
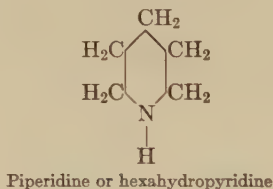
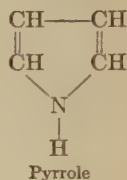
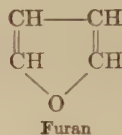
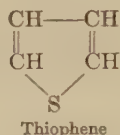
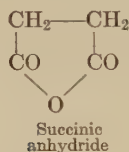
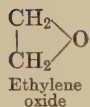
- Describe the preparation of the following compounds:

(a) α -naphthol	from naphthalene
(b) β -naphthol	" naphthalene
(c) α -naphthylamine	" naphthalene
(d) β -naphthylamine	" naphthalene
(e) tetralin	" naphthalene
(f) α -naphthoquinone	" naphthalene
(g) β -naphthyl methyl ether	" naphthalene
(h) α -nitroso- β -naphthol	" naphthalene
(i) 1-hydroxy-2-carboxynaphthalene	" naphthalene
(j) naphthionic acid	" naphthalene
(k) anthraquinone	" naphthalene
(l) anthraquinone	" anthracene
(m) β -aminoanthraquinone	" anthracene
(n) β -bromonaphthalene	" naphthalene

CHAPTER XXVIII

HETEROCYCLIC COMPOUNDS

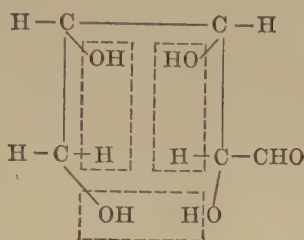
The cyclic or "ring" compounds so far considered, with a few exceptions, such as succinic anhydride and lactones, have contained the same elements within the ring (in this case, carbon atoms; hence carbocyclic). There are, however, very many compounds containing "cycles" in which elements other than carbon are also present; these are known as **heterocyclic** compounds; for example:



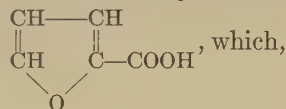
Furan, $\begin{array}{c} \text{CH}=\text{CH} \\ || \quad || \\ \text{CH} \quad \text{CH} \\ | \quad | \\ \text{O} \end{array}$, or furfuran, occurs in pinewood tar. Its most im-

portant derivative is **furfural**, $\begin{array}{c} \text{CH}=\text{CH} \\ || \quad || \\ \text{CH} \quad \text{C}-\text{CHO} \\ | \quad | \\ \text{O} \end{array}$, or furfuraldehyde, which

may be obtained from pentose sugars or pentosans when boiled with hydrochloric or sulfuric acid:



This serves as the basis for the detection and estimation of pentoses and pentosans. Commercially, furfural is prepared from corn cobs, oat hulls, and other waste cereal products rich in pentoses or pentosans. It is used in the manufacture of synthetic resins, disinfectants, deodorizers, solvents, paint and varnish remover, etc. The general properties of furfural are similar to those of benzaldehyde and formaldehyde. On oxidation, we get furoic acid or pyromucic acid,



as its name implies, may also be prepared by heating mucic acid, $\text{COOH} \cdot (\text{CHOH})_4 \cdot \text{COOH}$, an oxidation product of galactose or lactose. (The *Molisch* test for carbohydrates is dependent upon the production of furfural or its derivatives.)

Furfuryl alcohol, $\begin{array}{c} \text{CH}-\text{CH} \\ || \quad || \\ \text{CH} \quad \text{C}-\text{CH}_2\text{OH} \\ \diagdown \quad \diagup \\ \text{O} \end{array}$, is prepared by catalytic hydro-

genation of furfural. It is used as a solvent and for the manufacture of synthetic resins.

Pyrrole, $\begin{array}{c} \text{CH}-\text{CH} \\ || \quad || \\ \text{CH} \quad \text{CH} \\ \diagdown \quad \diagup \\ \text{N}-\text{H} \end{array}$, is present in coal tar and in bone oil (*Dippel's* oil),

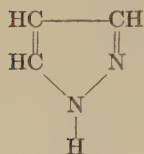
which is a product of the destructive distillation of bones. It may be prepared by distilling the ammonium salt of mucic acid. The pyrrole ring is present in chlorophyll (p. 383), in hemoglobin (p. 386), and in a number of alkaloids (p. 366). Pyrrole may be reduced to **pyrrolidine**,

$\begin{array}{c} \text{CH}_2-\text{CH}_2 \\ | \quad | \\ \text{CH}_2 \quad \text{CH}_2 \\ \diagdown \quad \diagup \\ \text{N}-\text{H} \end{array}$, a carboxylic acid derivative of which is **proline**,

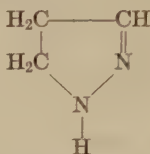
$\begin{array}{c} \text{CH}_2-\text{CH}_2 \\ | \quad | \\ \text{CH}_2 \quad \text{CH} \cdot \text{COOH} \\ | \quad | \\ \text{N}-\text{H} \end{array}$, one of the decomposition products of proteins. Pyr-

role compounds may be obtained from the destructive distillation of leather scrap and of gelatin.

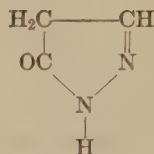
Other nitrogen-containing compounds are:



Pyrazole

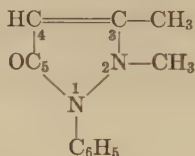


Pyrazoline (dihydropyrazole)

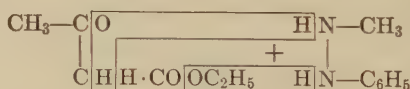


Pyrazolone

A derivative of the last compound is **antipyrine**:




or 2,3-dimethyl-1-phenyl-5-pyrazolone, which is made by condensing acetoacetic ester with methyl phenylhydrazine:

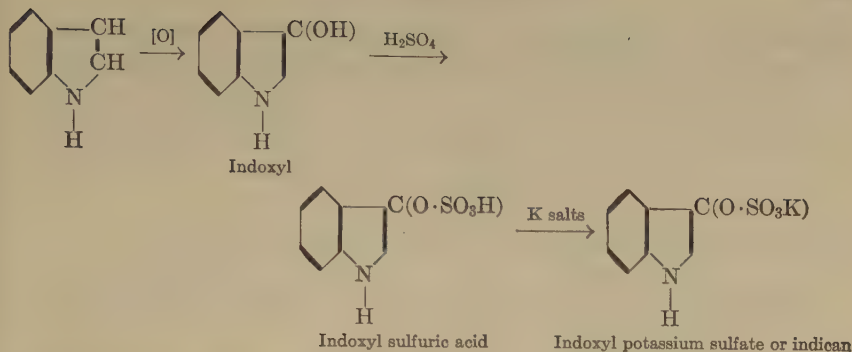


Antipyrine is used as an antipyretic and analgesic. The 4-dimethyl-amino derivative of antipyrine, known as "pyramidon," is used for similar purposes.

Phenyl methyl pyrazolone is used in photography and is known as "developer Z."

Indole, , represents a condensation of the benzene and pyrrole

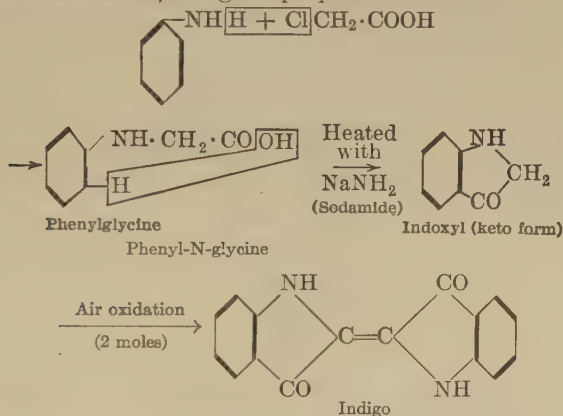
rings, and is an intestinal product formed when proteins putrefy. Indole is a highly toxic substance; it is detoxified by being converted into indican, in which form it is eliminated in the urine:



The amount of indican in the urine is a rough indication of the extent of putrefaction within the intestine.

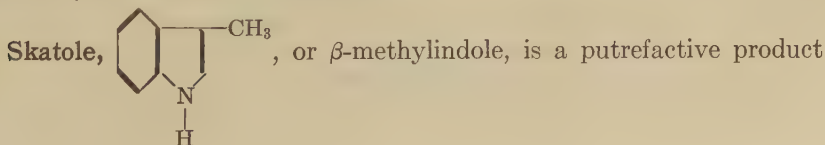
Indigo is a natural product obtained from the indigo plant (where it occurs as a glucoside), which grows in tropical countries; it is one of the oldest and best-known vat dyes. Its synthesis in the chemist's laboratory by *Baeyer* ranks as one of the great achievements in the history of organic chemistry.

On a commercial scale, indigo is prepared as follows:

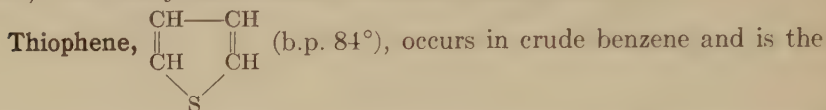
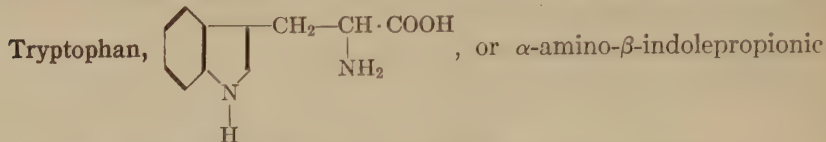


Despite the fact that more than a thousand chemically different dyes are now in commercial production, indigo has maintained its position as the leader in quantity.

The disodium salt of indigodisulfonic acid, known also as "indigo carmine," is used as a food color.



formed in the intestine, and its fate in the body is similar to that of indole. It is present in feces and has an extremely disagreeable odor.

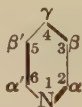


mother substance of many sulfur-containing compounds. It is separated from benzene by repeated extraction with H_2SO_4 , and may be identified by the "indophenin" reaction (in which a mixture of isatin, thiophene, and H_2SO_4 gives a blue color). The thiophene nucleus is part of the biotin molecule (p. 395).

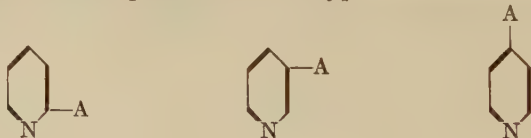


CH is replaced by N), is found in coal tar in the "light oil" fraction, in tobacco smoke, in *Dippel's* oil, and in crude ammonia. Pyridine is soluble in water, the solution being slightly alkaline in reaction. It has a characteristic, putrid odor and is an extremely stable substance, not being attacked by chromic acid (CrO_3) or nitric acid. It is used to denature alcohol. The pyridine ring is present in a number of alkaloids.

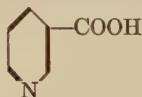
The positions in pyridine are numbered



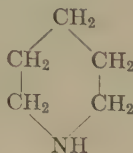
The compound behaves much like an aromatic compound and has three monosubstitution products of the type



Two important derivatives of pyridine are **nicotinic acid** (p. 394),




which is pyridine-3-carboxylic acid, and **pyridoxine**, (p. 394). When reduced, pyridine yields **piperidine**, a substance which occurs in pepper and has a pepperlike odor.

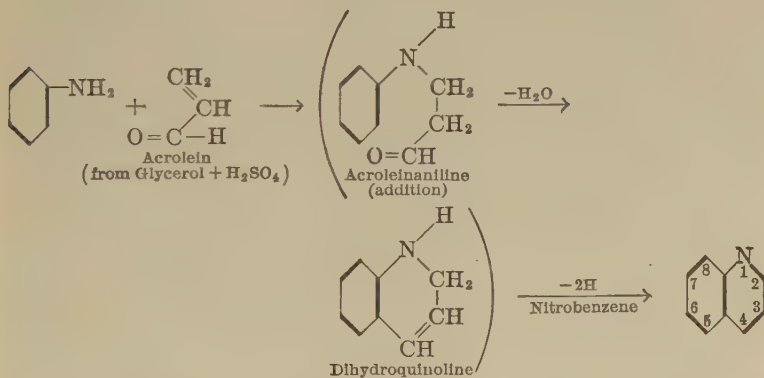


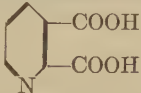
Pyridine is a weak base and forms quaternary compounds with acids and organic halides:



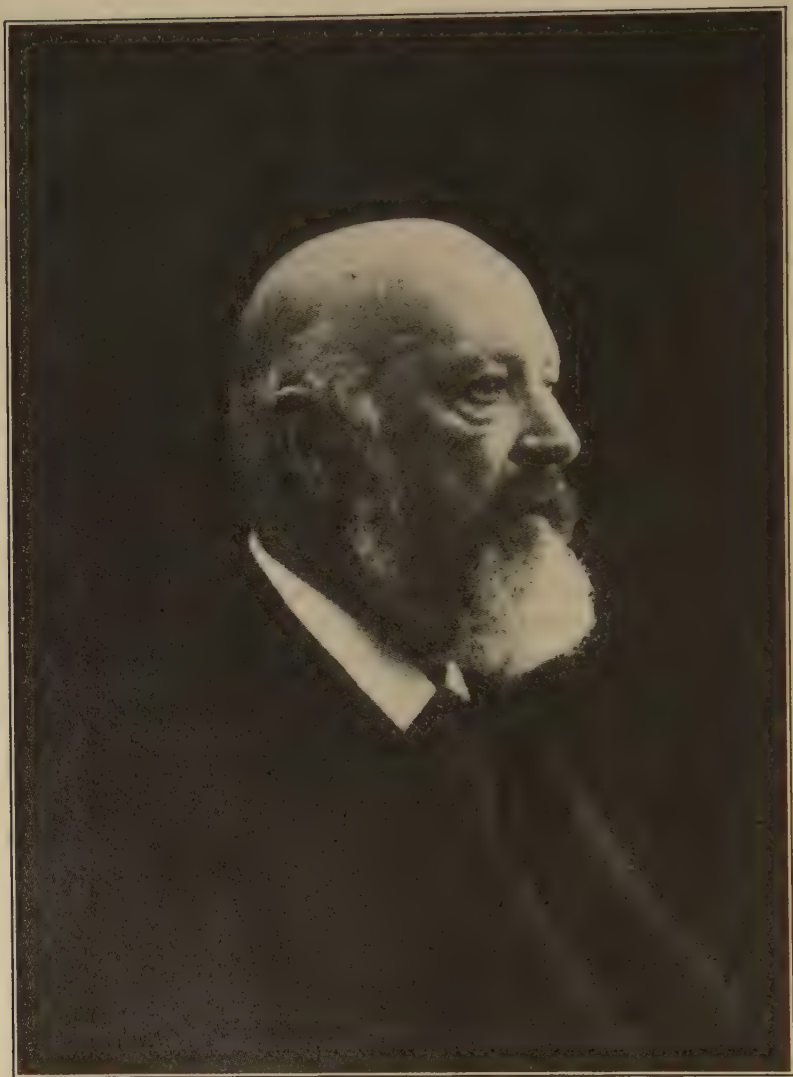
Quinoline, , a condensation of one benzene and one pyridine

ring, is present in coal tar and bone oil, and may be prepared by the *Skraup* reaction, in which a mixture of aniline, glycerol, H_2SO_4 (dehydrating agent), and nitrobenzene (oxidizing agent) is heated:



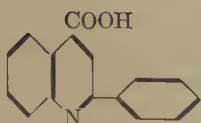
On oxidation with permanganate in the presence of iron, quinoline yields quinolinic acid, .

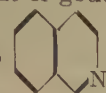
The quinoline ring is present in certain alkaloids. A quinoline derivative known as "plasmochin" is used as a remedy for malaria. 8-Hydroxyquinoline is used in the quantitative determination of metals, especially aluminum.

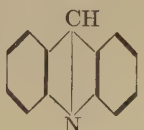


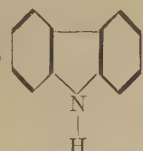
JOHANN FRIEDRICH WILHELM ADOLF BAEYER (1835-1917)

Responsible for the synthesis of indigo, was one of the most fruitful workers in organic chemistry during the nineteenth century.

Cinchophen, , 2-phenyl-4-carboxyquinoline, is useful in the treatment of gout.

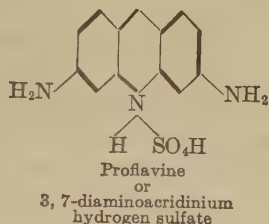
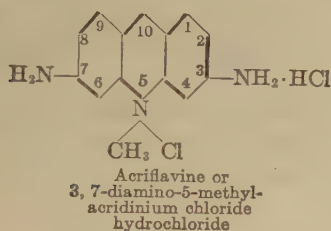
Isoquinoline, , is found in coal tar. (The isoquinoline grouping is present in a number of alkaloids.)

Two other nitrogen heterocyclic compounds are **acridine**, ,

present in coal tar, and **carbazole**, , or dibenzopyrrole, pres-

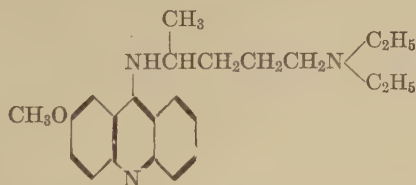
ent in anthracene oil. Carbazole is used in the manufacture of dyes, explosives, insecticides, etc.

Two important derivatives of acridine have been introduced in medicine:




They are strongly antiseptic and non-toxic.

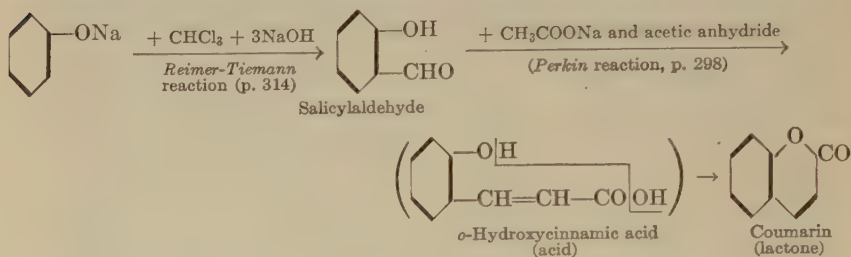
Atabrine, another acridine derivative,



is a remedy for malaria; atabrine and plasmochin (p. 337) are the two best synthetic substitutes for quinine, a material of strategic importance in global war.

Coumarin, , is the sweet-smelling constituent of tonka bean

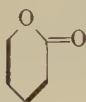
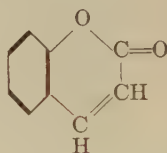
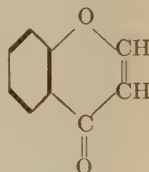
and freshly mown hay. It is used extensively in flavoring extracts, flavoring tobacco, perfumery, and, mixed with synthetic vanillin, in artificial vanilla mixtures. It is made by the following series of reactions:



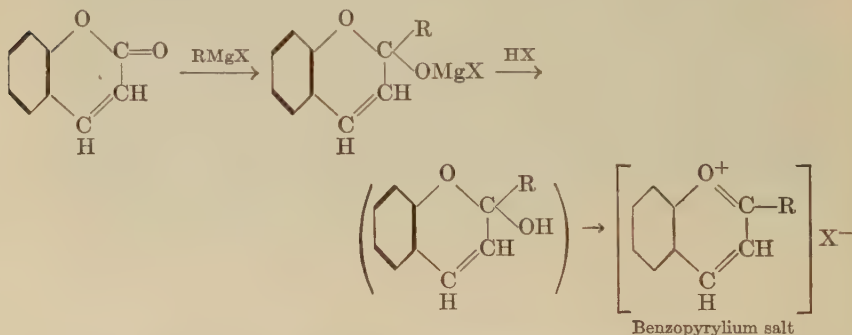
Coumarin is also benzo- α -pyrone.



Pyran

 α -Pyrone γ -PyroneBenzo- α -pyrone
or coumarinBenzo- γ -pyrone
or chromone

By a *Grignard* synthesis, coumarin can be converted to a hydroxy compound or "pseudo base," which, although it cannot be isolated, readily forms "pyrylium" salts with acids:



Salts of this type are assumed to represent the acid (red) forms of anthocyanidines (p. 385). The stability of such oxonium salts can be accounted for by the possibility of several resonating structures.

QUESTIONS

1. Indicate what is meant by a heterocyclic and a carbocyclic compound. What elements commonly enter the ring to form heterocyclic compounds?
2. Write structural formulas for the following: (a) furan; (b) pyrrole; (c) thiophene; (d) furfural; (e) pyridine; (f) pyrrolidine; (g) quinoline; (h) indole; (i) coumarin; (j) indigo; (k) acridine; (l) isoquinoline; (m) phthalimide; (n) pyromucic acid; (o) α -methylpyridine; (p) pyrazole; (q) 8-hydroxyquinoline; (r) N-methylpyrrole; (s) nicotinic acid; (t) carbazole; (u) furfuryl alcohol.
3. Describe the preparation of the following compounds:

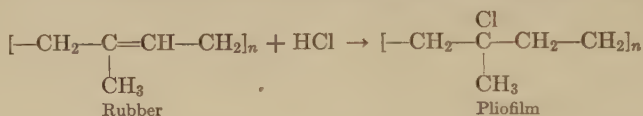
(a) furfural	from xylose
(b) quinoline	" aniline
(c) coumarin	" phenol
(d) indigo	" aniline
(e) antipyrine	" acetoacetic ester

CHAPTER XXIX

SYNTHETIC PLASTICS AND SYNTHETIC RUBBERS

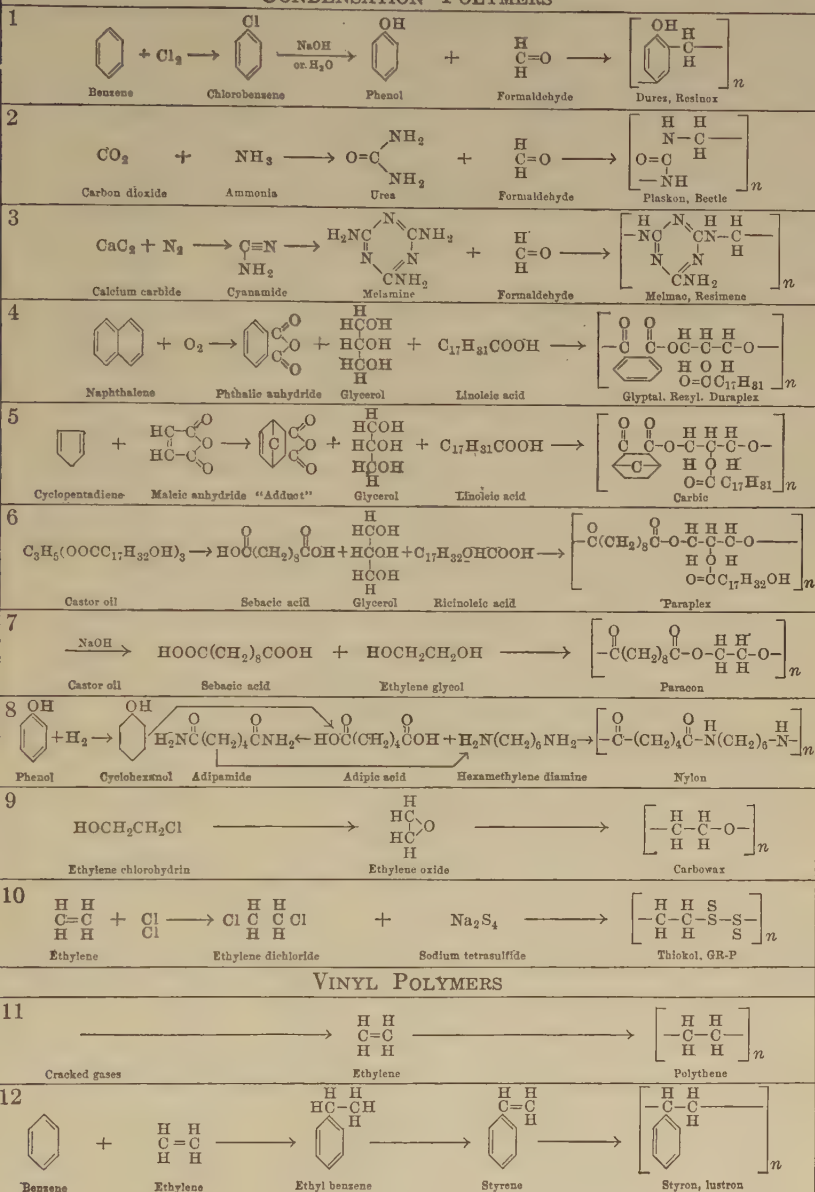
In various parts of the book the subject of polymerization has been discussed. In the following table the possible structures of some of the more useful polymers are given.¹

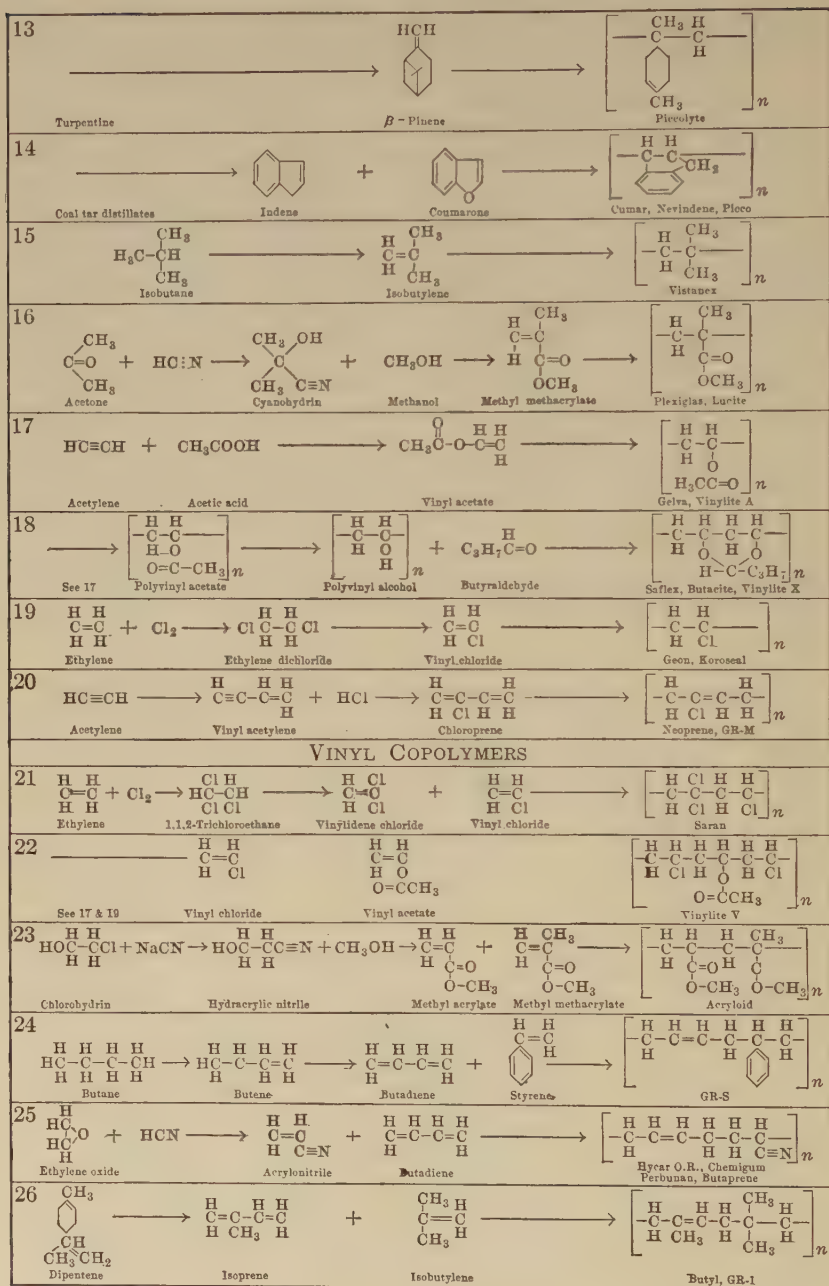
Several additional useful plastics are made by treating natural polymers (such as cellulose, rubber, or rosin) with a variety of reagents; e.g.,



¹ For this information we are indebted to P. O. Powers, *Chem. & Eng. News*, **22**, 1992 (1944).

CONDENSATION POLYMERS





CHAPTER XXX

DYES AND STAINS

DYES

Dyes have a wide application. They are applied to cotton, linen, silk, wool, paper, straw, wood, leather, feathers, hair, fats, waxes, soaps, inks, food (jams, macaroni, candy), condiments, varnishes, paints, etc. In analytical chemistry, dyes are used as indicators (e.g., phenolphthalein, congo red, methyl orange). In histology and bacteriology, they are used for staining microscopical preparations (e.g., methylene blue, acid fuchsin, safranin, eosin, gentian violet, neutral red, Bismarck brown). Dyes are also used as explosives (picric acid, picrates, trinitro-cresols, etc.); in photography (eosin, erythrosin, etc.); and as antiseptics (acriflavine, proflavine, malachite green, mercurochrome, etc.).

Dyes have been used from the very earliest times. Until the middle of the last century, those employed for dyeing and printing were the vegetable dyes, coloring substances from certain insects (as cochineal) and molluscs, and a number of mineral colors. In 1856, *Perkin*, in attempts to prepare quinine artificially, found that aniline (a coal-tar product) could be oxidized with chromic acid to yield a violet dye, to which was given the name "mauve." This was the first coal-tar dye to be prepared, but since then no less than 3000 dyes derived from coal-tar products have appeared on the market.

The dyes, then, may be either "natural" or "artificial." Among the natural ones, logwood, fustic, Brazil wood, turmeric, and natural indigo still find uses. The artificial dyes, however, play a much more important part in the industries. Those of particular value are "fast" to light, rubbing, and washing.

Dyes are also classified in accordance with their behavior towards fabrics as "substantive" or "direct," and "adjective" or "mordant," dyes. The direct dye can be applied directly (without a mordant) to the fabric, usually silk or wool. The adjective or mordant dye needs a "go-between"—a third substance which attaches itself to the fabric on the one hand, and the dye on the other; this third substance is the "mordant" ("bite into"), e.g., various aluminum, chromium, and iron salts and



WILLIAM HENRY PERKIN (1838-1907)

Prepared the first coal-tar dye, "mauve" (p. 353), and is therefore called the "father" of the coal-tar dye industry.

tannic acid. The combination of a mordant and a dye is known as a color "lake," the color of the lake varying with the choice of mordant. By using different mordants with the same dye, various colored lakes are produced. Mordant dyeing is mainly used for cotton goods. In direct dyeing, the fabric is immersed directly in the prepared dye bath, heated to the required temperature, and agitated for a certain length of time.

In this volume we cannot go into the various theories which have been suggested to explain the process of dyeing, beyond merely enumerating them: the chemical theory—that the dye combines with the components of the fabric or certain constituents of the cell; the mechanical theory, based on adsorption; the solution theory, somewhat like the theory of the solution of one metal in another, as in an alloy; and the colloid theory, based on the colloidal properties of the reacting substances.

From the practical standpoint, the classification of dyes depends upon their behavior towards fibers. Dyes are divided into:

1. *Acid dyes*, which include nitro compounds and the sodium salts of sulfonic and carboxylic acids. These are direct dyes for wool and silk (in an acid bath) but are not adapted for the dyeing of cotton. The usual method is to boil the material with the color solution in the presence of Glauber's salt and dilute sulfuric acid. These dyes fade rapidly when the fabric is washed with soap or washing powders, but are resistant or "fast" to the effects of sunlight.

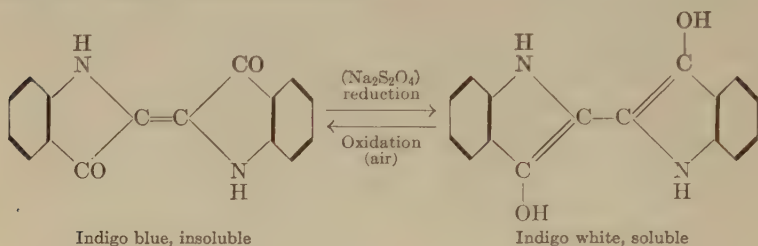
2. *Basic dyes*, substances which combine readily with acids to form salts. They are "direct" dyes for silk, artificial silk, and wool, but not for cotton and linen. The last two have first to be "mordanted," with an acid mordant, such as tannic acid, since the dye itself is basic. Fabrics dyed with basic dyes fade when exposed to sunlight. The basic dyes owe their basicity to the presence of an amino group, and usually appear on the market as hydrochlorides, zinc double salts, oxalates, etc. The basic dyes were the first coal-tar colors, mauve itself being a basic dye.

3. *Direct cotton dyes*, usually sodium salts of sulfonic and carboxylic acids and generally containing the azo (—N=N—) grouping. They are adsorbed by the fiber directly and are used mainly for dyeing cotton material (in the presence of NaCl or Na_2SO_4).

4. *Sulfur dyes*—produced from various aromatic organic compounds by the action of sulfur and sodium sulfide. They are used for dyeing cotton and are fairly "fast" to washing.

5. *Vat dyes*—these dyes are first reduced (generally with sodium hyposulfite, usually called sodium hydrosulfite, $\text{Na}_2\text{S}_2\text{O}_4$), the fabric being

then agitated in the soluble reduced dye bath and exposed to the air, oxidation causing the precipitation of the insoluble dye. Examples of such dyes are indigo and anthraquinone dyes. They are very stable, being the "fastest" colors known.



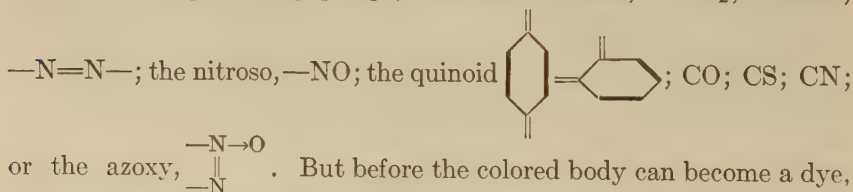
The famous Tyrian purple, which was obtained centuries ago from a Mediterranean mollusc, is a dibromoindigo.

The effect of constitution on color is illustrated even more markedly by thioindigo, in which a change of NH to S yields a red dye, but a change of only one NH in indigo to S yields *Ciba violet* (red + blue).

6. *Mordant dyes*, which are generally phenolic or acidic. Mordants must be used to fix the dye to the fabric. Examples of mordant dyes are the coloring matters of dye woods (such as logwood and fustic) and alizarin.

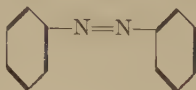
7. *Ingrain dyes* include substances, like aniline black and para red, which are really formed in the dye bath as a result of the chemical combination of two or more compounds. They are mainly cotton dyes.

The classification just described is a somewhat empirical one as it arose in response to the practical needs of the dyer. Another classification, a more scientific one, is based on the groups present in the molecule of the dyestuff. All dyes, in the first place, contain one or more **chromophore** or color-producing groups, such as the nitro, —NO_2 ; the azo,



it must also possess either acidic or basic characteristics, so that it can attach itself to the fiber or to the tissue (within the cell). These acidic or basic properties are given to the dye when **auxochrome** groups are

present, such as OH, SH, NH_2 , NHR , or NR_2 . For example, azobenzene,



which is a colored compound, is not a dye; but *p*-dimethylaminoazobenzene,

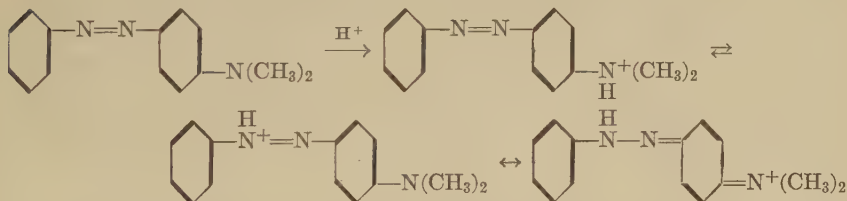


is a dye.

The relation between color and chemical constitution has been studied for a long time; the chromophore-auxochrome theory of *Witt* is still the most satisfactory one. From the modern electronic point of view, further generalizations have been based on the assumption that absorption of visible light (color) is connected with the oscillation of valence electrons (*Lewis* and *Calvin*); the greater the number of mobile electrons and the greater their mobility or deviation from the normal structure, the stronger the absorption of light. In other words, conjugation and the existence of resonating forms with marked shifts in polar charge will cause the appearance of color in molecules.

Although chromophores are associated with color, auxochromes are necessary to provide dyeing properties. These same groups are also required to furnish resonating forms in which the charges shift a great deal.

To refer to the example given previously, the addition of the auxochrome $-\text{N}(\text{CH}_3)_2$ enables us to write resonating structures:

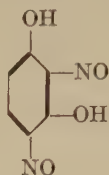


The entire subject of dyes is so extensive that only a few members of the class can be mentioned here. However, one generally accepted classification of dyes will be given, and each type will be illustrated by one or more examples of dyes, stains, or indicators in use. (The student should make a point of noting the presence of chromophore and auxochrome groups in these compounds.)

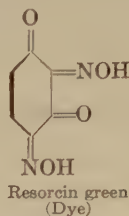
CLASSES OF DYE STUFFS

EXAMPLES

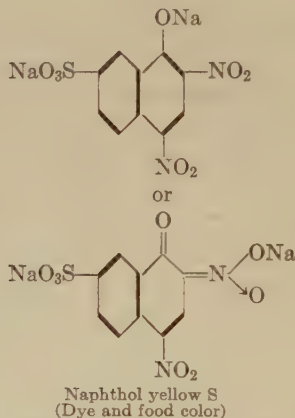
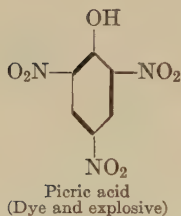
Nitroso dyes



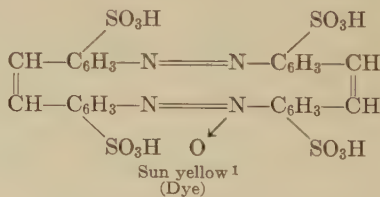
or



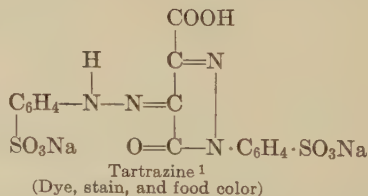
Nitro dyes



Stilbene dye

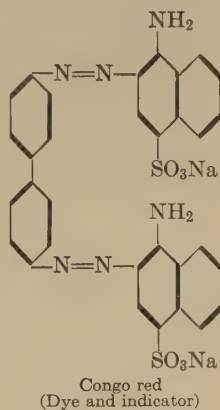
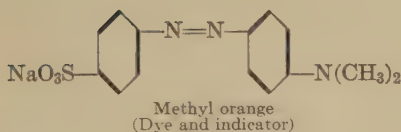
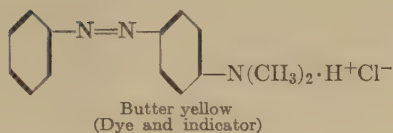
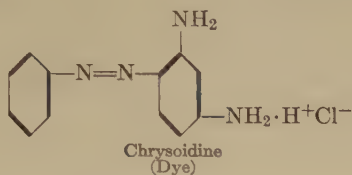


Pyrazolone dyes

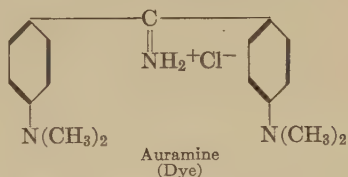


¹ Notice the presence of the sulfonic acid grouping, or of its salt, as part of the structure of some of these dyes. The presence of this group increases the solubility of the dye in water.

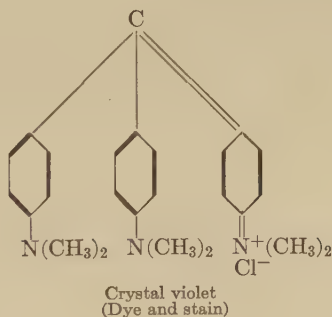
Azo dyes



Diphenylmethane dyes

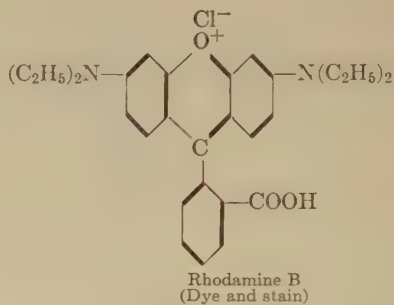


Triphenylmethane dyes

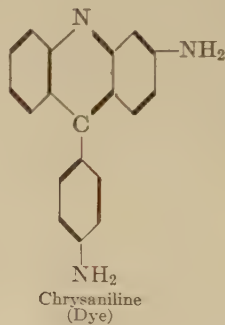


This class includes the phthaleins (p. 301). *p*-Rosaniline is the corresponding triaminotriphenylmethane derivative. Rosaniline (fuchsin, magenta) has, in addition, one CH_3 group *o*- to one NH_2 .

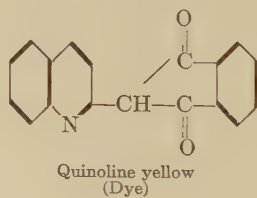
Xanthene dyes



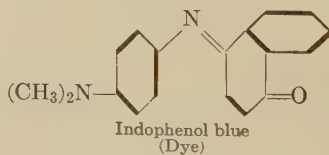
Acridine dyes



Quinoline dyes



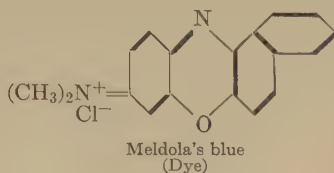
Indophenol dyes



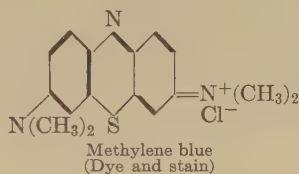
CLASSES OF DYESTUFFS

EXAMPLES

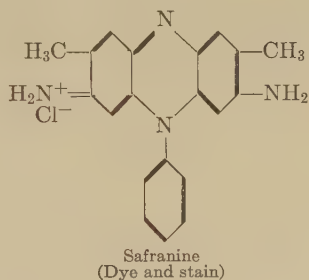
Oxazine dyes



Thiazine dyes

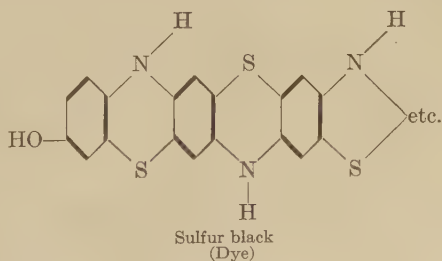


Azine dyes



This structure minus the two methyl groups represents *Perkin's mauve*.

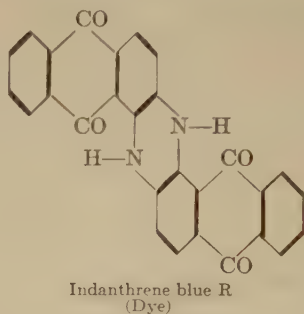
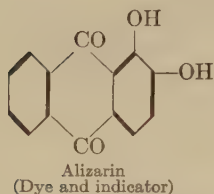
Sulfur dyes



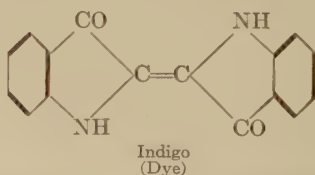
CLASSES OF DYESTUFFS

EXAMPLES

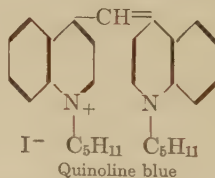
Anthraquinone dyes



Indigo dyes

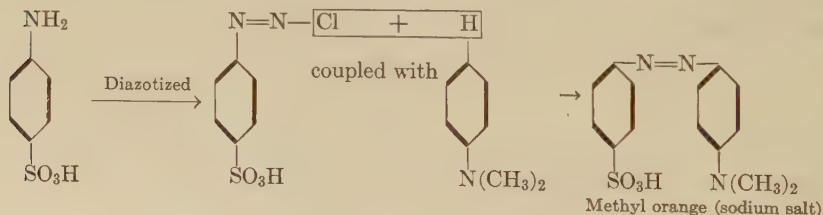


Cyanine dyes



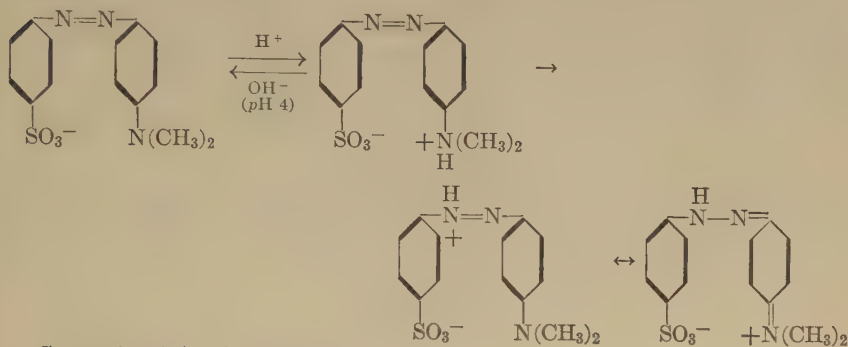
Some of these dyes increase the sensitivity of photographic emulsions to yellow and red light by absorbing such light.

The preparation of dyes cannot be described here, but the principles employed in the synthesis of some of them will be illustrated.

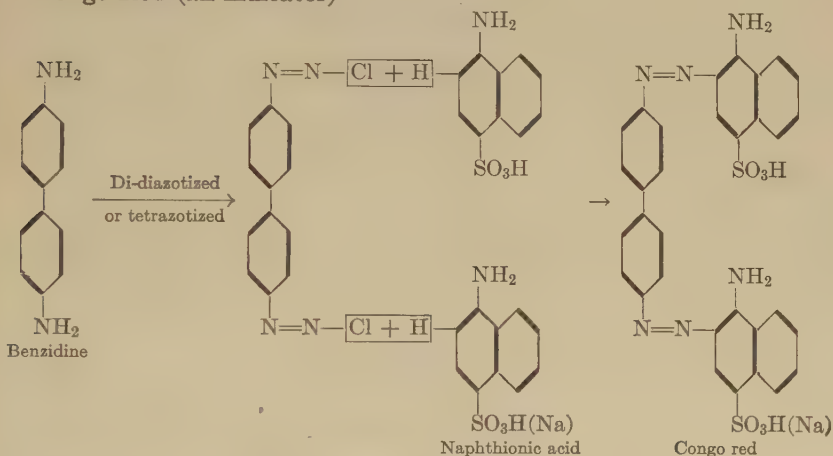
Methyl Orange

This formulation of the synthesis uses classical formulas and does not indicate the changes of structure which are assumed to take place when a colored dye is formed from colorless or slightly colored substances.

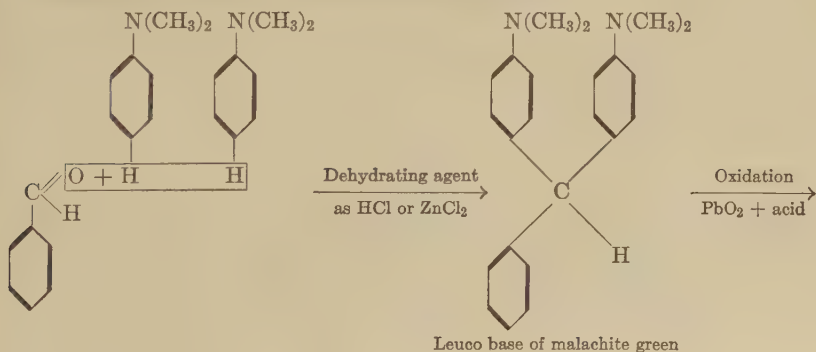
In this particular synthesis we are dealing with an indicator, that is, a compound which actually undergoes a change of color during a reaction (acid-base indicators change at a definite pH). This means, of course, several intramolecular changes in structure to account for the changes in color.

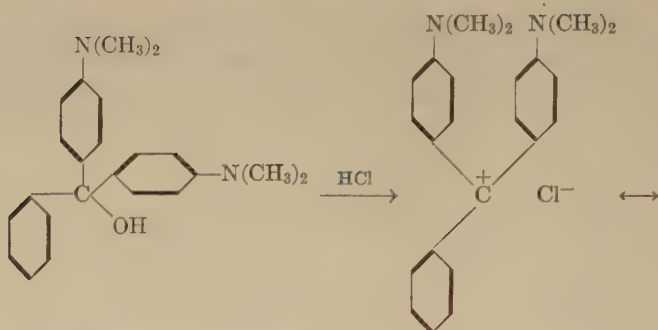


Congo Red (an indicator)

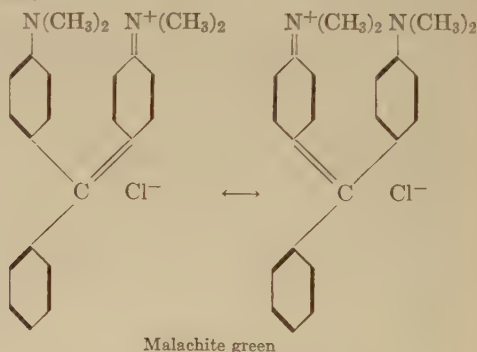


Malachite Green, a triphenylmethane dye



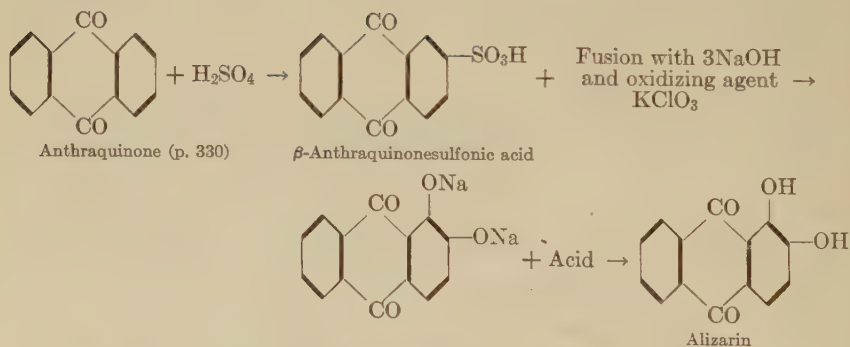


Color base of malachite green (colorless)



Malachite green

Alizarin,



Dyes used in medicine as antiseptics, in chemotherapy, etc., include the following classes: azo, acridine, and triphenylmethane.

STAINS

Dyes have come into use in bacteriology because very often various bacteria can be differentiated by "staining" them with dyes. A stain is a dye or any other substance which colors tissues so that they can be submitted to microscopic examination.

Basic aniline dyes are the common type of stains; these show special affinity for the nuclei of cells. Acid dyes are also used; these generally have a selective affinity for the protoplasm. Some of the most commonly employed aniline dyes are methylene blue, gentian violet, fuchsin, crystal violet and safranine.

The chemistry of the process involved in staining is probably not unlike that of dyeing; there may be a chemical combination between the dye and the protoplasm of the cell, or a process of adsorption, or possibly both processes.

QUESTIONS

1. Indicate what is meant by the following terms: (a) acid dye; (b) basic dye; (c) direct cotton dye; (d) mordant dye; (e) sulfur dye; (f) vat dye; (g) azo dye; (h) food color; (i) fast dye; (j) color lake; (k) chromophore groups; (l) auxochrome groups; (m) chromogen; (n) triphenylmethane dye; (o) anthraquinone dye; (p) leuco base; (q) color base.
2. Describe the preparation of the following dyes:

(a) picric acid	from benzene
(b) methyl orange	" aniline
(c) congo red	" benzene
(d) malachite green	" toluene
(e) alizarin	" naphthalene
(f) indigo	" aniline

CHAPTER XXXI

TERPENES AND RELATED SUBSTANCES

The terpenes are complex hydrocarbons, usually with the formula $C_{10}H_{16}$, present in, or obtained from, such substances as camphor, oil of turpentine, and particularly "essential oils." "Essential oils" are the products obtained when certain plants (like the conifer and citrus varieties), barks, leaves, or flowers are distilled with steam or pressed or extracted with organic solvents. Most of them are sweet-smelling substances containing a number of related organic compounds and are extensively used as flavors, in perfumery, and in medicine.

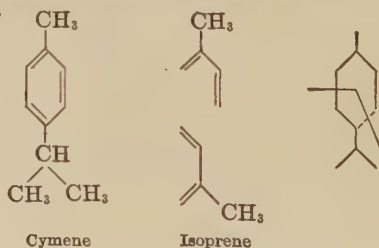
The compounds classified as terpenes fall into several classes:

- C_5H_8 —hemiterpenes.
- $C_{10}H_{16}$ —terpenes (true terpenes).
- $C_{15}H_{24}$ —sesquiterpenes.
- $(C_{10}H_{16})_x$ —polyterpenes.

The only hemiterpene C_5H_8 is **isoprene**, which is obtained by the distillation of rubber, by the pyrolysis of turpentine, or by synthesis. It is made from the pentanes of petroleum and is also formed as a by-product in the catalytic preparation of butadiene from petroleum fractions. As we know, it polymerizes to rubber, and most of the successful synthetic rubbers are polymers or copolymers of homologous diolefins.

Isoprene also occupies an important place among the terpenes and some other naturally occurring substances, because it may be considered the parent monomer of all their structures.

The terpenes, $C_{10}H_{16}$, are hydroaromatic hydrocarbons closely related to the aromatic cymene (*p*-methylisopropyl benzene). Every terpene contains this same carbon skeleton which is in effect a combination of two isoprene nuclei.

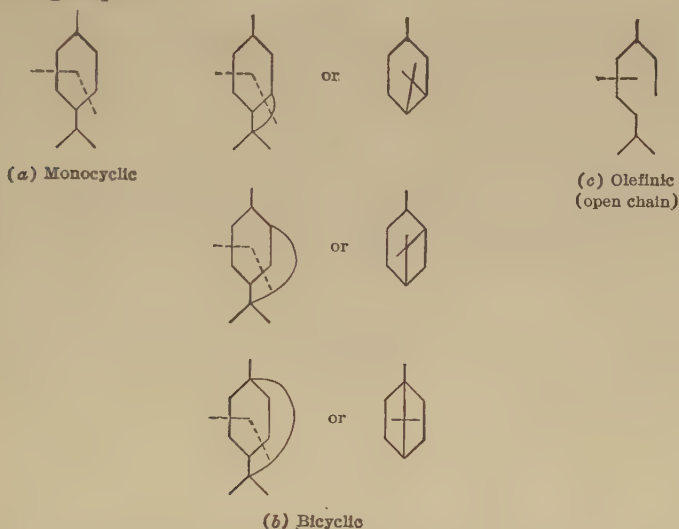


The lines cutting across bonds show the relationship to isoprene.

These structural relationships have naturally led to speculations on the origin of terpenes in plants, possibly through the intermediary formation of isoprene from even simpler molecules.

In general, the chemical behavior of the terpenes is that of alicyclic compounds. They show olefinic unsaturation and add the usual reagents, including bromine and chlorine, hydrogen halides, nitrosyl chloride ($\text{NO}-\text{Cl}$), and nitrogen tetroxide. Their double bonds are oxidized by ozone, dilute aqueous KMnO_4 , and stronger oxidizers, such as nitric acid, which break down the molecule. Dehydrogenation, and, in some cases, dehydration, convert terpenes to the corresponding aromatic compounds.

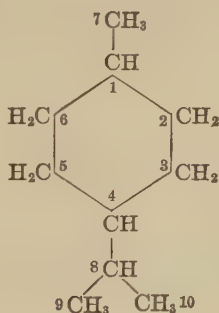
The terpenes and their derivatives can be classified into three general structural groups:



Some of the more important representatives of each group are the following:

(a) *Monocyclic Terpenes.*

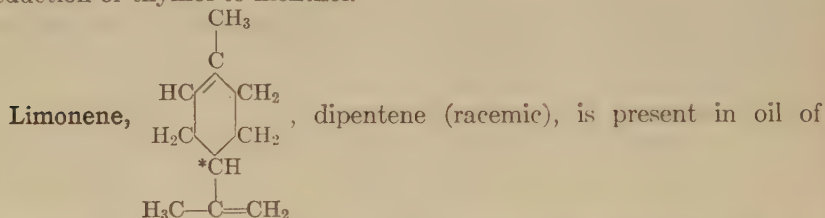
Menthane,



hexahydrocymene, does not occur in nature but is an important parent substance.

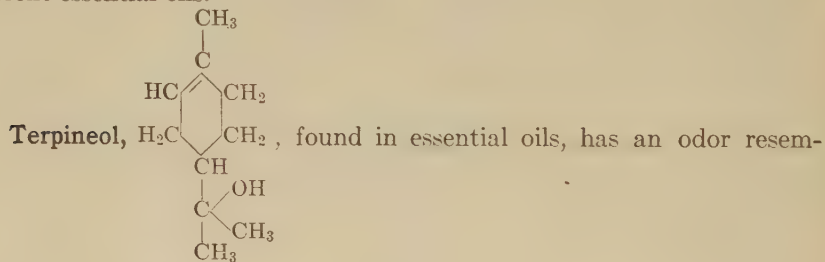
Menthol, 3-menthanol, occurs in oil of peppermint. It has a peppermintlike odor and finds extensive use as a flavoring agent. Even though the natural product is levorotatory,¹ the synthetic racemic (*dl*) menthol, obtained by catalytic hydrogenation of thymol (p. 280), is a possible substitute. The cresols are convenient raw materials for this synthesis.

Menthone, 3-menthanone, is also found in oil of peppermint. It is, of course, reducible to menthol, and it is an intermediate product in the reduction of thymol to menthol.

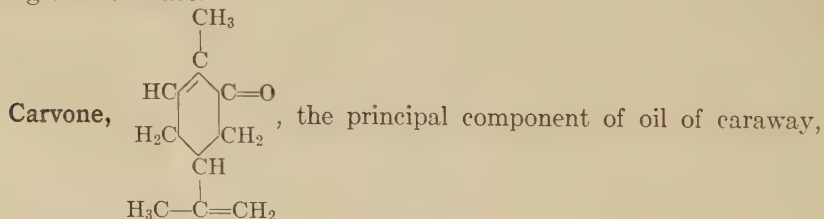


lemon, lime, etc. It is a dimer of isoprene, from which it has been obtained. This reaction can be viewed as a diene synthesis (p. 302). The reverse decomposition apparently takes place when pinene (p. 361), the main component of turpentine, yields isoprene on decomposition by heat.

Limonene, like most terpenes, exists in optically isomeric forms, the carbon marked * being asymmetric. The various forms occur in different essential oils.



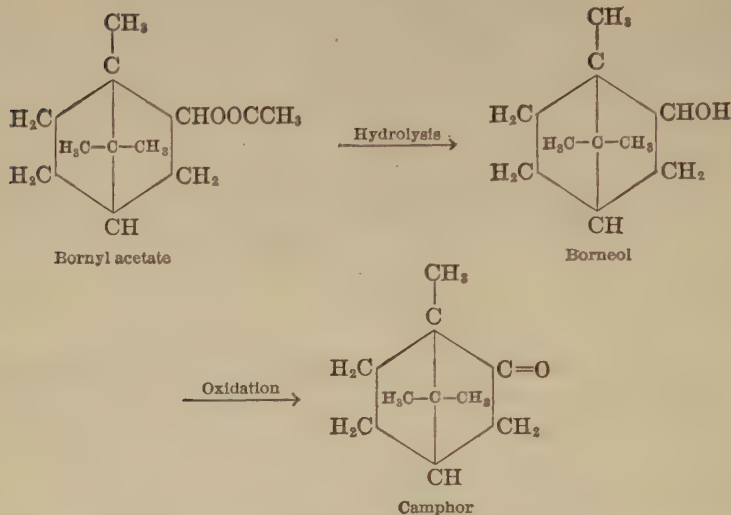
bling that of lilacs.



possesses the characteristic odor of this oil.

(b) *Bicyclic Terpenes.*

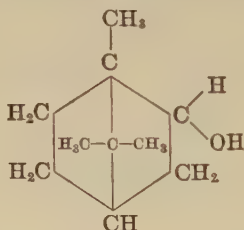
¹ Carbons 1, 3, and 4 are asymmetric. Four of the eight possible optically isomeric menthols are known.



The addition of HCl to pinene causes a molecular rearrangement.

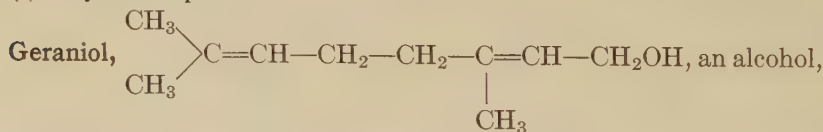
Camphor is used largely in the manufacture of celluloid and in pharmaceutical preparations. Among artificial camphors on the market are pinene hydrochloride and triphenyl phosphate (p. 279).

Borneol,

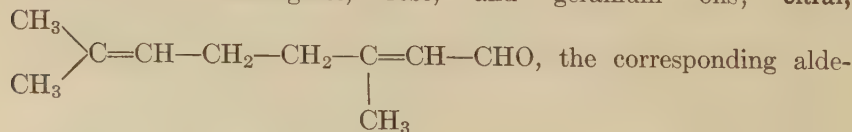


is the alcohol obtained from camphor by reduction. It occurs in nature, being known as "Borneo camphor," and has a camphorlike odor.

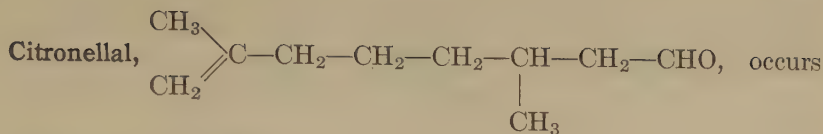
(c) *Olefinic Terpenes.*



is found in lemongrass, rose, and geranium oils; **citral**,

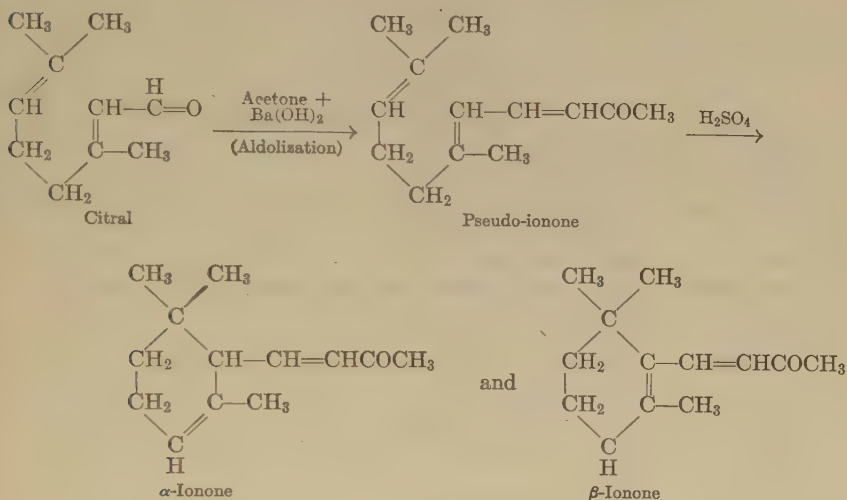


hyde, occurs in lemon and orange oils.



in the oil of citrus fruits.

Ionone, the first synthetic perfume, was produced in an attempt to synthesize the violet perfume substance. It is a mixture of two isomers.



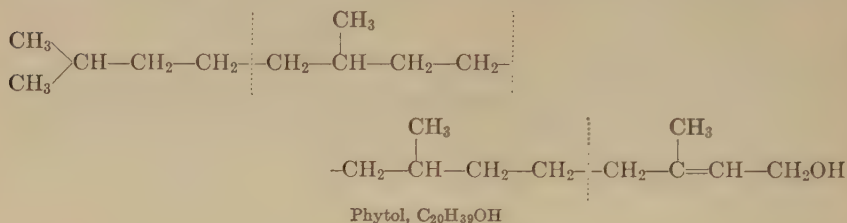
β -Ionone is a decomposition product of carotene (p. 392) and related substances; therefore, the β -ionone structure (or the corresponding acyclic nucleus) is a component of the structural formulas of these important natural products (vitamin A among them).

All that need be said about the sesquiterpenes and polyterpenes is that the fundamental skeletons are polymers of the isoprene nucleus:



Many important substances are closely related to the terpenes, including those so-called *polyenes* that are characterized by long conjugated chains and by color (plant pigments, p. 385), and **phytol**, an alcohol

which occurs in one of the ester groups of chlorophyll (p. 383) and in vitamin K (p. 398).



ESSENTIAL OILS

OIL	CHIEF KNOWN CONSTITUENTS
Allspice	Eugenol; sesquiterpene
Angelica root	Phellandrene; valeric acid
Angelica seed	Phellandrene; valeric acid
Anise	Anethole; anisaldehyde
Birch	Methyl salicylate
Bitter almond	Benzaldehyde; hydrocyanic acid; phenyloxyacetonitrile
Camphor	Camphor; borneol; pinene
Caraway	Carvone; <i>d</i> -limonene
Cedar wood	Cedrene; cedar camphor
Celery seed	Limonene; phenols
Cinnamon bark	Cinnamaldehyde; eugenol
Citronella	Geraniol; citronellal
Clove	Eugenol
Cognac	Esters of caprylic acid
Eucalyptus	Phellandrene; cineol
Fennel	Anethole; fenchone
Garlic	Allyl propyl disulfide; diallyl disulfide
Geranium	Geraniol; citronellol
Ginger	Phellandrene
Guaiac wood	Guaiacol
Hops	Humulene; geraniol; terpenes
Jasmine	Benzyl acetate; linaloöl
Juniper berries	Pinene; cadinene; juniper camphor
Lavender	Linalyl acetate; linalol
Lemon	Limonene; phellandrene; citral; citronellol; geranyl acetate; linaloöl
Lime	<i>d</i> -Limonene; citral; methyl anthranilate
Mustard	Allyl isothiocyanate
Neroli	Linalyl acetate; linaloöl; geraniol; limonene
Nutmeg	Myristicin; pinene
Onion	Allyl propyl disulfide
Orange	Limonene
Pepper	Phellandrene; dipentene
Peppermint	Menthol; menthyl esters; menthone
Rose	Geraniol; citronellol; geranyl acetate

OIL	CHIEF KNOWN CONSTITUENTS
Sassafras	Safrol; eugenol; camphor; pinene; phellandrene
Spearmint	Carvone; limonene; pinene
Thyme	Thymol; carvacrol; cymene; linaloöl; borneol
Tolu	Esters of benzoic and cinnamic acids
Turpentine	Pinene
Valerian	Borneol; bornyl formate, acetate and isovalerate; pinene; camphene
Wintergreen	Methyl salicylate
Ylang-ylang	Linaloöl; geraniol; benzoic esters; methyl ester of <i>p</i> -cresol.

Oil of chenopodium, an old household remedy for worms, is a mixture of various terpenes.

QUESTIONS

1. Write structural formulas for (a) pinene; (b) menthol; (c) camphor; (d) geraniol; (e) β -ionone.
2. What is the source of rosin? What are its important uses? What important acid does it contain?
3. Write the carbon skeletons characteristic of (a) monocyclic terpenes; (b) bicyclic terpenes; (c) olefinic terpenes; (d) sesquiterpenes.

CHAPTER XXXII

ALKALOIDS

The alkaloids are basic nitrogenous substances which occur in plants, usually in combination with organic acids (citric, tartaric, oxalic, malic, tannic, etc.), and are characterized by powerful physiological activity. They contain the elements C, H, N or C, H, O, and N, and are complex in constitution, generally containing pyrrole, pyrrolidine, pyridine, quinoline, or isoquinoline rings in their structure. Only a very brief presentation of the subject can be given here.

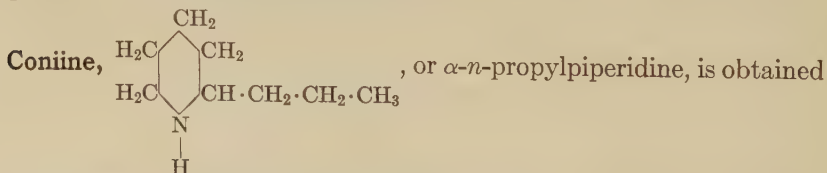
Alkaloids occur in dicotyledonous plants, poppy for example. Most of them are crystalline solids (coniine and nicotine are liquids), and most of them are levorotatory. They are insoluble in water, soluble in alcohol, ether, chloroform, etc., to a greater or less extent, form water-soluble salts with acids, have a bitter taste, and some are excessively poisonous. Most of the alkaloids are used in the form of salts, such as hydrochloride, nitrate, bisulfate, sulfate, or phosphate.

The following substances, known as "alkaloidal reagents," precipitate alkaloids from their aqueous or acid solutions: tannic acid, potassium-mercuric iodide ($KI + HgI_2$), phosphomolybdic acid, picric acid, and phosphotungstic acid. (The "alkaloidal reagents" are quite often used to precipitate proteins.)

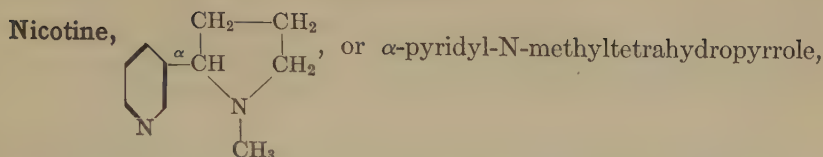
Color reactions are frequently used to identify certain alkaloids.

The method of extraction from plants often consists of extracting with acidified (HCl or H_2SO_4) water and reprecipitating with bases.

The number of alkaloids known is very large; only a few of the more important ones can be mentioned here.



from the seeds of spotted hemlock and has been produced synthetically. It is very poisonous and has a disagreeable odor and an acrid taste. Chemically, it is the simplest alkaloid.



present in tobacco leaves, is used as an insecticide. The oxidation of nicotine with HNO_3 or KMnO_4 yields nicotinic acid, a vitamin (p. 394).

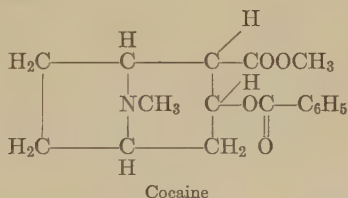
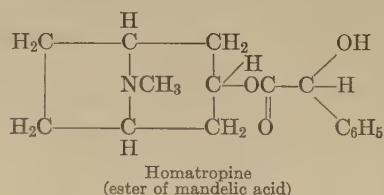
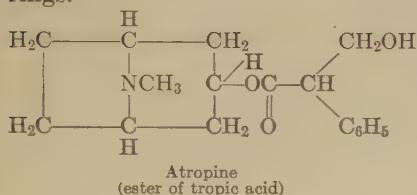
Piperine, $\text{C}_{17}\text{H}_{19}\text{NO}_3$, occurs in pepper, from which it is extracted. Piperidine (p. 337) is a decomposition product of piperine.

Atropine, $\text{C}_{17}\text{H}_{23}\text{NO}_3$, obtained from the *deadly nightshade* (*belladonna*), is used as a mydriatic (dilating the pupil) in ophthalmic surgery.

Homatropine, an artificial alkaloid derived from atropine, dilates the pupil more rapidly than atropine and the effect is not as lasting.

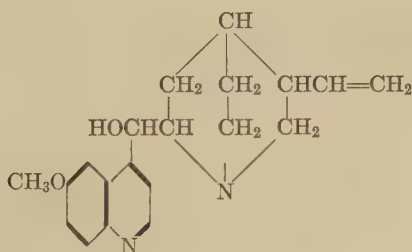
Cocaine, $\text{C}_{17}\text{H}_{21}\text{NO}_4$, is contained in coca leaves. It is used as a local anesthetic in minor operations, though, owing to its extremely toxic properties, it has been largely replaced by novocaine, butyn, etc.

The characteristic structure common to the last three compounds is the so-called tropane nucleus, a fusion of piperidine and pyrrolidine rings.



Two important quinoline alkaloids from cinchona bark are quinine and cinchonine.

Quinine,



is obtained from cinchona bark, etc. It is used in the treatment of malaria, a widely spread disease which assumed added importance in World War II. A synthesis of quinine was announced in 1944.

Cinchonine, $C_{19}H_{22}N_2O$, from cinchona bark, resembles quinine in its physiological properties, though its effects are not so pronounced.

Strychnine, $C_{21}H_{22}N_2O_2$, and **brucine**, $C_{23}H_{26}N_2O_4$, occur together in the seeds of *nux vomica* and in *St. Ignatius'* beans. Strychnine is an extremely poisonous substance, acting on the spinal cord and producing characteristic convulsions. In very small doses, it is used as a tonic, to increase the appetite, as a heart stimulant, and in various forms of paralysis. Brucine acts similarly.

Morphine, $C_{17}H_{19}NO_3$, is the chief alkaloid of opium (which is the dried juice of the seed capsules of a variety of poppy). It is used as an analgesic and a soporific.

Heroin is a diacetyl derivative of morphine. Its effects are, in general, similar to those of morphine. It is used as a sedative and to lessen coughing.

Narcotine, $C_{22}H_{23}NO_7$, and **codeine**, $C_{18}H_{21}NO_3$, are also present in opium and are closely related to morphine.

Dionine is an artificial alkaloid made from morphine (ethyl morphine) and is used to produce sleep and relieve pain.

The morphine alkaloids contain the isoquinoline nucleus.

Pilocarpine is the active principle obtained from the leaves of *Pilocarpus jaborandi*, a Brazilian shrub. It is used principally to increase perspiration.

Emetine, the active alkaloid of ipecac, is used in the treatment of amoebic dysentery.

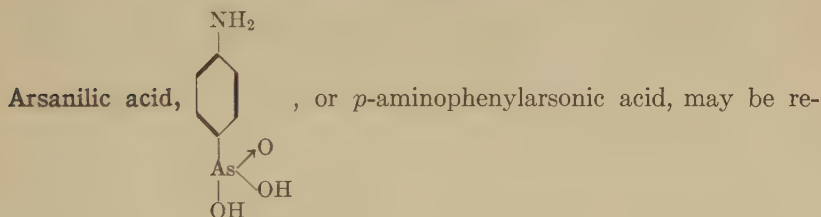
The alkaloids, of which only a few representatives have been named, comprise the last large group of naturally occurring organic compounds in our survey. They may be related in the living organisms to the purines and pyrimidines, which are also nitrogen heterocycles. Proteins are another class of natural nitrogenous substances. The non-nitrogenous groups include, of course, the carbohydrates, the fats, and the terpenes.

CHAPTER XXXIII

ARSENIC, MERCURY, AND BISMUTH COMPOUNDS OF THE AROMATIC SERIES

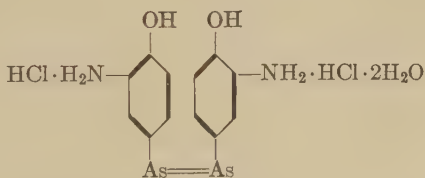
Arsenic and mercury compounds, particularly the arsenic, have found wide application in the treatment of diseases caused by protozoans (such as syphilis). The organic combinations of these metals have an advantage over the inorganic compounds in that they are less toxic to mammals and more toxic to protozoan parasites.

ARSENIC COMPOUNDS



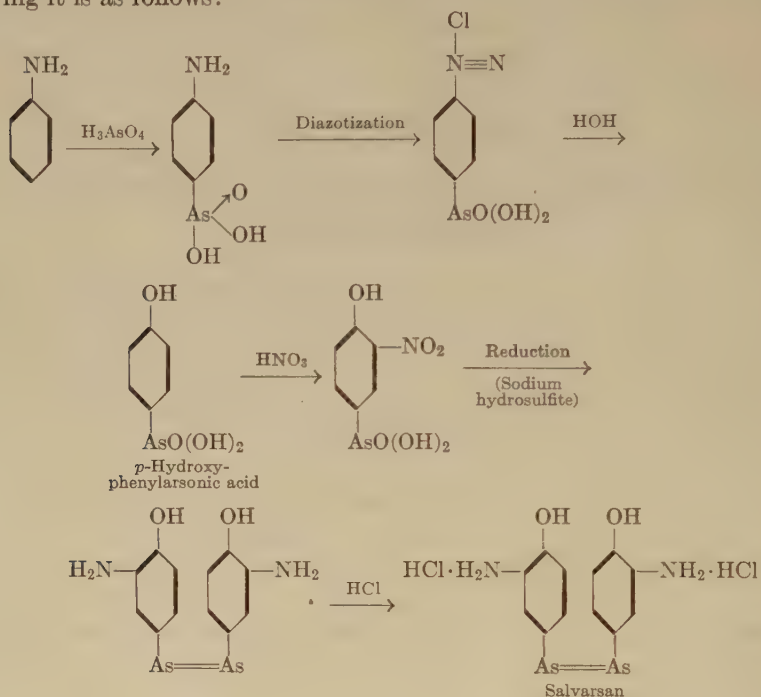
garded as being derived from arsenic acid, $\text{AsO}(\text{OH})_3$, in which one OH group is replaced by aniline, and is prepared by combining aniline with arsenic acid. The monosodium salt is known as "atoxyl" and "soamin" and, though used at one time in the treatment of syphilis, relapsing fever, etc., is now chiefly of interest as an intermediate in the preparation of salvarsan.

Salvarsan,



or 3,3'-diamino-4,4'-dihydroxyarsenobenzene dihydrochloride, known also as **arsphenamine** and "606," was first synthesized by *Ehrlich* and

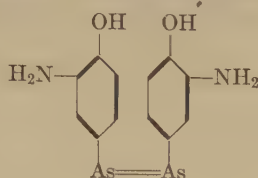
introduced by him for the treatment of syphilis. One method of preparing it is as follows:



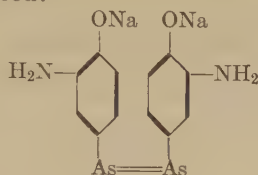
Although we cannot, in this book, enter into a prolonged discussion regarding the interesting question of the effect of chemical structure upon physiological action, *Ehrlich's* discovery of salvarsan deserves a few words of comment. When *Ehrlich* first began his celebrated research, he was aware of the fact that trypanosomes—a group of parasites—are killed by a number of dyes and a number of organic arsenic compounds, of which atoxyl was the most important. This compound contains pentavalent arsenic. The important discovery was made that, although it would cure animals of trypanosomiasis, it had no toxic action upon trypanosomes *in vitro*. After many trials with many arsenical compounds, *Ehrlich* was in a position to formulate this general rule: that only compounds containing trivalent arsenic were effective in killing trypanosomes, and that the effectiveness of compounds containing pentavalent arsenic depended upon their reduction in the body to the trivalent form. The most efficient substances were found to be compounds containing trivalent arsenic joined to a benzene ring and containing also an amino group. This was later still further improved upon by the discovery that the most effective compounds were those contain-

ing an OH group in the *p*-position, an amino group, and arsenic—as in salvarsan itself.

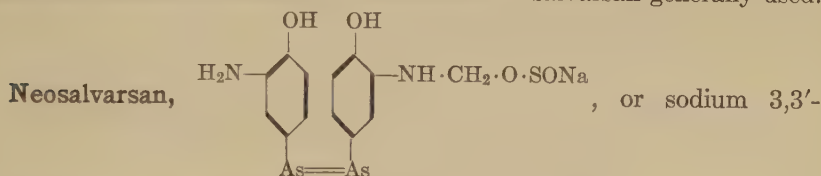
Salvarsan, that is the dihydrochloride salt, is soluble, but it forms an acid solution, and is irritant and toxic. By the addition of two molecules of NaOH to one of salvarsan, the neutral base is obtained:



This is insoluble. Upon the further addition of two molecules of NaOH, the sodium salt is produced:



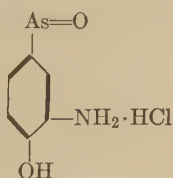
and this is soluble in water. It is the form of salvarsan generally used.



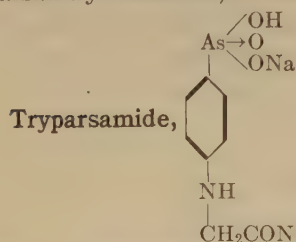
diamino-4,4'-dihydroxyarsenobenzene-*N*-methylenesulfinate, is also known as **nearsphenamine** or "914" and was introduced by *Ehrlich* because of its greater solubility than salvarsan. It is prepared by combining salvarsan with sodium formaldehyde sulfoxylate ($\text{HOCH}_2\cdot\text{OSONa}$).

Silver salvarsan and silver neosalvarsan have the same uses as salvarsan, but it is claimed that the presence of silver in the molecule raises the toxicity to parasites without increasing the toxicity to mammals.

Mapharsen, *m*-amino-*p*-hydroxyphenylarsine oxide hydrochloride,



is also used in the treatment of syphilis. It may be produced from salvarsan by oxidation, or converted into salvarsan by reduction.



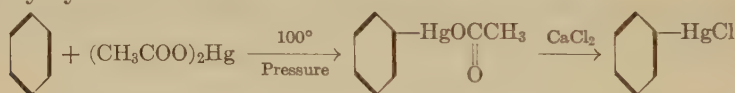
, has been successfully applied in the treat-

ment of human sleeping sickness. It is also used in resistant cases of syphilis.

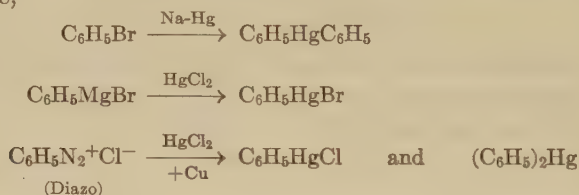
$(\text{C}_6\text{H}_5)_2\text{As} \cdot \text{Cl}$, diphenylchloroarsine, is used as a "sneeze" gas in warfare.

MERCURY COMPOUNDS

Mercuration of the aromatic nucleus is a typical substitution reaction which yields important intermediates and many valuable antiseptics and disinfectants. The mercury-containing group can be introduced directly by substitution:

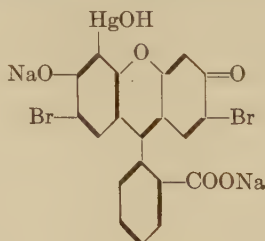


or indirectly by double decomposition with various types of derivatives; for example,

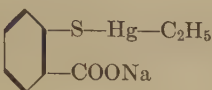


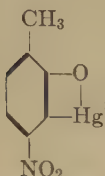
These compounds are useful in the preparation of other derivatives and of pharmaceuticals such as the following:

Mercurochrome,



also called *merbromin*, a mercurial derivative of fluorescein, is an active germicide.

Merthiolate, , a derivative of salicylic acid; **meta-**

phen, , a derivative of *o*-cresol; and **merphenyl nitrate**,

$C_6H_5HgNO_3 \cdot C_6H_5HgOH$, are other examples of mercuric compounds used as antiseptics and disinfectants.

BISMUTH COMPOUNDS

Bismuth compounds of indefinite structure are used in the treatment of a number of diseases. In several instances, they have replaced mercurials in the treatment of syphilis. Among the simpler of these bismuth salts are derivatives of tartaric and salicylic acids.

QUESTIONS

1. Outline the preparation of salvarsan from benzene.
2. Write structural formulas for (a) arsanic acid; (b) tryparsamide; (c) neosalvarsan; (d) mapharsen; (e) mercurochrome.

CHAPTER XXXIV

A BRIEF OUTLINE FOR THE IDENTIFICATION OF ORGANIC COMPOUNDS

The identification of an organic compound is not a simple matter. We have no methods quite as clearly defined as those of inorganic chemistry.

In the identification of an organic compound, the first step is to make certain that the compound is in a pure state—a fact which may very often be established by determining the sharpness of the boiling point or melting point.

In the next place, an elementary analysis should indicate the elements present in the compound. Once these are determined, certain limits are immediately set as to the kind of compound it can be. For example, a compound which, upon analysis, shows the elements C, H, and O only, cannot be an amine.

The classification of organic compounds which depends on their most characteristic reactions is intimately bound up with the presence, within the molecules of these compounds, of various functional groups, such as OH, NH_2 , or COOH . In this chapter the attempt will be made to give a brief résumé of some of the reactions used for identifying such groups. Incidentally, this chapter ought to serve, to some extent, as a review.

Hydrocarbons. Usually, these are colorless gases, liquids, or solids, insoluble in water and soluble in alcohol and ether. Sometimes the analysis reveals only carbon and hydrogen. The paraffin hydrocarbons are inert substances. The olefins and acetylenes decolorize bromine water and are oxidized by dilute aqueous permanganate to form saturated compounds, but only acetylenes form metallic acetylides. The aromatic hydrocarbons may, as a rule, be nitrated to form nitro derivatives. If the aromatic compounds contain a side chain (a CH_3 group, for example), the side chain can be oxidized (by chromic acid or potassium permanganate or dilute nitric acid) to the carboxyl group. The hydrocarbons with condensed benzene nuclei (such as naphthalene and anthracene) are solids and may be identified by their oxidation products and, very often, by the fact that they form well-defined picrates (with picric acid) with definite melting points. The terpene hydrocarbons

(such as pinene) present many difficulties when attempts are made to isolate them. Sometimes physical properties (boiling point, density, specific rotation, etc.) prove helpful.

Halogen Compounds. The aliphatic compounds are almost non-ionizable and practically insoluble in water. The alkyl chlorides are lighter than water; the bromides and iodides are heavier. They are hydrolyzed to the corresponding alcohols. With the aromatic halides, where the halogen is attached to the benzene nucleus, we get substances which are either liquids or solids, with a faint, agreeable odor, and insoluble in water. They are stable compounds and do not, for example, react with alkali. They are utilized in the *Fittig* and *Grignard* syntheses. The aromatic halogen compounds with the halogen in the side chain behave similarly to the aliphatic halogen compounds and possess lachrymatory properties.

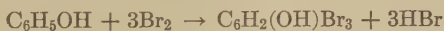
Alcohols. Most of the monohydroxy alcohols are colorless liquids, neutral in reaction; some have a characteristic odor and taste. The solubility in water decreases with increasing molecular weight. The polyatomic alcohols are oily liquids or crystalline solids, soluble in water, and less soluble, or altogether insoluble, in ether.

Primary alcohols when oxidized (with chromic acid, for example), give first an aldehyde and then an acid; secondary alcohols yield ketones; and tertiary alcohols break down into carboxylic acids containing fewer carbon atoms than the original compound. The carbonyl compounds can be used to identify the alcohols from which they are formed.

The OH group is very often identified by forming esters with acid chlorides or anhydrides. Solid esters make convenient derivatives. Many of these esters have characteristic odors. By submitting such esters as the acetates to a quantitative hydrolysis, it becomes possible to determine whether the original compound contains one or more OH groups. (For every OH group, one acetyl group is used.)

Phenols are usually crystalline solids. (The solubility in water increases with the number of OH groups present in the ring.) They are weak acids, reacting with alkalies to form salts. They are too weak to react with sodium bicarbonate solution.

Nearly all phenols give a precipitate of a polybromophenol when treated with bromine water; e.g.,



and yield deeply colored solutions with ferric chloride. Many give the *Liebermann* test (a deep blue or green color, when the phenol is dissolved in cold concentrated H_2SO_4 and a little NaNO_2 added). (This test is also used to identify the nitroso group.)

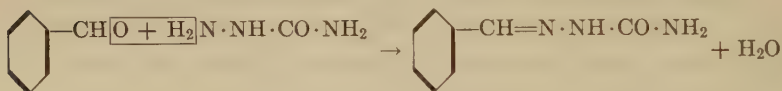
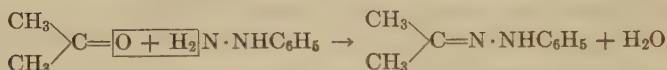
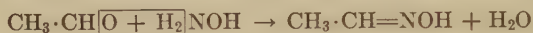
Phenols, like alcohols, combine with acetic anhydride to form esters; with acyl chlorides they also form esters which can be identified by their melting or boiling points; e.g.,



Ethers are neutral, chemically inactive liquids. They are often identified by their boiling points, or by the following reaction:



Aldehydes and Ketones. The lower aldehydes are liquids possessing a characteristic odor; unlike ketones, they reduce *Fehling's* or ammoniacal silver nitrate solution. For purposes of identification, aldehydes and ketones may be treated with hydroxylamine to form oximes, with phenylhydrazine or substituted phenylhydrazines to form phenylhydrazones, and with semicarbazide (aminourea) to form semicarbazones; e.g.,



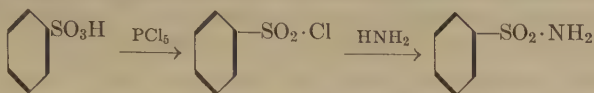
Most aldehydes give the *Schiff* test (restoring the pink color to a solution of magenta which has been decolorized with SO_2).

Carboxylic Acids. The lower aliphatic monobasic acids (as formic and acetic) are liquids, soluble in water, but the solubility decreases with increasing molecular weight. The higher members (like palmitic and stearic) are solids, insoluble in water. The aliphatic polybasic acids (like oxalic and succinic) are solids, soluble in water. Many of the aromatic acids (like benzoic and *o*-toluic) are not very soluble in cold, but more so in hot, water. This provides a simple means of crystallization.

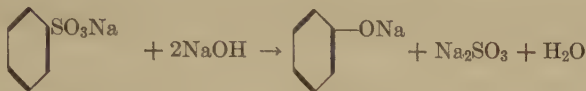
The acidity of the substance may be determined by titrating with standard alkali. The conversion of an acid to a solid ester and the elimination of the carboxyl group (in the form of CO_2) by heating with soda lime are helpful in identifying the acid. Often the acid is converted to its acyl chloride. These chlorides are easily converted to esters or amides (with ammonia or amines), very useful derivatives.

Aromatic Sulfonic Acids. As a rule, these are soluble substances, difficult to crystallize. For purposes of identification, the corresponding

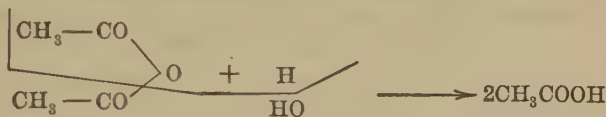
amide is prepared by first forming the sulfonyl chloride with PCl_5 and then converting this chloride to the amide with a definite melting point.



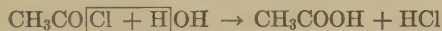
Fusion with alkali to form the corresponding phenol is also sometimes employed:



Acid Anhydrides. As a rule, the aliphatic compounds are colorless liquids, insoluble in water and soluble in alcohol and ether. The aromatic compounds are solid. They are usually identified by hydrolyzing them to the corresponding acids or salts; e.g.,



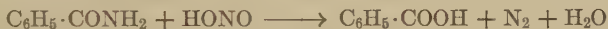
Acyl halides are pungent-smelling liquids, easily convertible (hydrolysis) into the corresponding acids; e.g.,



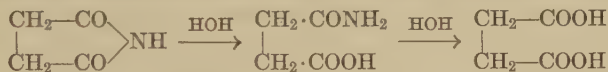
Acid amides are, as a rule, well-defined, crystalline substances. They can be hydrolyzed with boiling alkali to the corresponding acids (salts); e.g.,



or

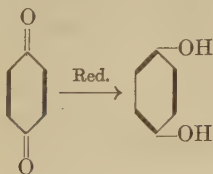


Acid imides, like the amides, are hydrolyzed by boiling with alkalis:



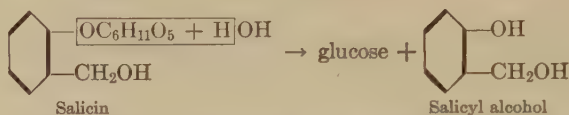
Esters are volatile compounds, insoluble in water, with agreeable odors. The esters may be saponified with alkali.

Quinones are colored compounds (yellow or red). Some are volatile with steam. As a rule, quinones can be reduced:



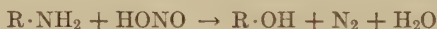
Carbohydrates. These are solids soluble in water (except the polysaccharides, such as starch, etc.). Among the polysaccharides, starch gives a blue color, and glycogen and the dextrins a violet to a violet-red, with iodine. The sugars (lactose, maltose, galactose, levulose, glucose) reduce *Fehling's* solution and form osazones with phenylhydrazine. Sucrose or cane sugar is a notable exception. The sugars are optically active.

Glucosides, on hydrolysis, yield glucose, in addition to one or more substances; e.g.,

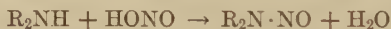


Amines. The lower members of the aliphatic amines (like methylamine) are flammable gases, with an odor resembling that of ammonia; the higher members (like butylamine) are liquids. With acids they form salts soluble in water and in alcohol. The aromatic amines are either liquids (like aniline) or solids (like diphenylamine).

With aliphatic amines, nitrous acid converts a primary amine into one or more alcohols:



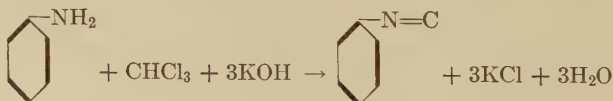
a secondary amine is converted into the yellow nitrosoamine:



and a tertiary amine forms salts.

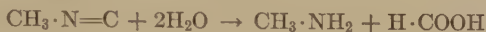
With the aromatic amines, the manner in which nitrous acid behaves will be dependent upon whether the NH_2 group is in the nucleus or in the side chain. If the amino group is in the nucleus, diazonium salts are formed (in the cold) which are converted to phenols on heating, or to azo dyes on coupling with phenols or aromatic amines; if the NH_2 group is in the side chain, then the compound behaves like an aliphatic amine. With secondary aromatic amines, nitrous acid yields nitroso derivatives similar to those obtained with aliphatic secondary amines. A tertiary amine such as dimethylaniline reacts with HONO to produce *p*-nitrosodimethylaniline.

The primary amines, whether aromatic or aliphatic, give the carbylamine reaction (the isocyanide is formed, which has a highly disagreeable odor); e.g.,

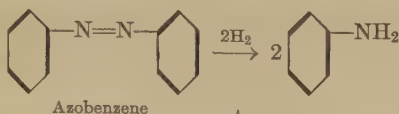


Nitro Compounds. Usually, these are oily liquids or solids, insoluble in water and dilute HCl. They are identified by being reduced to the corresponding amines.

Cyanides and Isocyanides. The cyanides are liquids or solids with an agreeable odor. They are hydrolyzed to the corresponding acids and are reduced to the primary amines. On hydrolysis the isocyanides yield formic acid and an amine; e.g.,



Azo compounds are colored solids and include a large class of important dyes. They yield, on reduction, amino compounds; e.g.,



Purines, of which uric acid and caffeine are examples, are not easily identified. Most of them give the *murexide* test: the substance is evaporated to dryness with concentrated HNO_3 and is made alkaline with ammonia or NaOH; a violet or red color is produced.

Alkaloids are mostly solids (nicotine and coniine are exceptions), soluble in alcohol, somewhat less soluble in ether, chloroform, and benzene, and usually insoluble in water. Most of them are levorotatory. They dissolve in acids, forming salts, and are precipitated by alkalies. Alkaloids are not easily identified, but as a class they are precipitated by the "alkaloidal reagents," such as tungstic, phosphomolybdic, tannic, and picric acids, and potassium-mercuric iodide. Many of them are identified by color reactions with H_2SO_4 and an oxidizing agent.

Sulfur Compounds. The aromatic sulfonic acids have already been discussed. The only other sulfur compounds that need be mentioned here are the mercaptans, e.g., $\text{C}_2\text{H}_5\text{SH}$, and the sulfides, e.g., $(\text{C}_2\text{H}_5)_2\text{S}$; both types of compounds have very disagreeable odors.

Terpenes and Allied Compounds. These substances are flammable, mostly volatile, possess characteristic odors, and are insoluble in water but soluble in many organic solvents. They do not behave as aliphatic or aromatic compounds, and they are, as a rule, complex in structure. Derivatives are usually prepared in order to identify them.

Proteins are complex substances consisting, in the main, of amino acid units. They are identified by a number of color tests. With *Millon's* reagent (mercuric nitrate containing nitrous acid) most of them give a red color or precipitate. When heated with HNO_3 , a yellow

color is developed which is changed to orange on the addition of ammonia (*xanthoproteic* reaction). When proteins are mixed with a strong solution of KOH and a drop or two of CuSO_4 solution, a violet color is obtained (*biuret* reaction).

GENERAL SOLUBILITIES OF CLASSES OF ORGANIC COMPOUNDS

Generalizations. A solvent dissolves those compounds which are chemically closely allied to it. Homologs are mutually soluble.

Hydrocarbons and their halogen substitution products are either insoluble or only very slightly soluble in water. They dissolve in alcohol, ether, benzene, etc.

The solubility of a compound in water increases with the increase of oxygen content; especially is this true when the oxygen atoms are combined with hydrogen as in —OH groups.

The homologs of low molecular weight of the aliphatic series (up to about 5 carbons), such as alcohols, aldehydes, ketones, amines, and acids, are soluble in water; but the solubilities decrease with increasing molecular weight.

Alkali salts of acids, salts of amines, sugars, polybasic acids, hydroxy acids, sulfonic acids, and polyhydroxy alcohols are soluble in water (all polar compounds).

Esters are very slightly soluble in water, but soluble in alcohol and ether.

Ether dissolves very many organic compounds. (Not salts of acids or other polar compounds.) It is slightly soluble in water and is used for extracting products from aqueous solutions.

Acid anhydrides are soluble in alcohol and ether.

Fats and oils are insoluble in water, but readily soluble in benzene, ether, chloroform, etc.

Nitro compounds are insoluble in water but soluble in alcohol and ether.

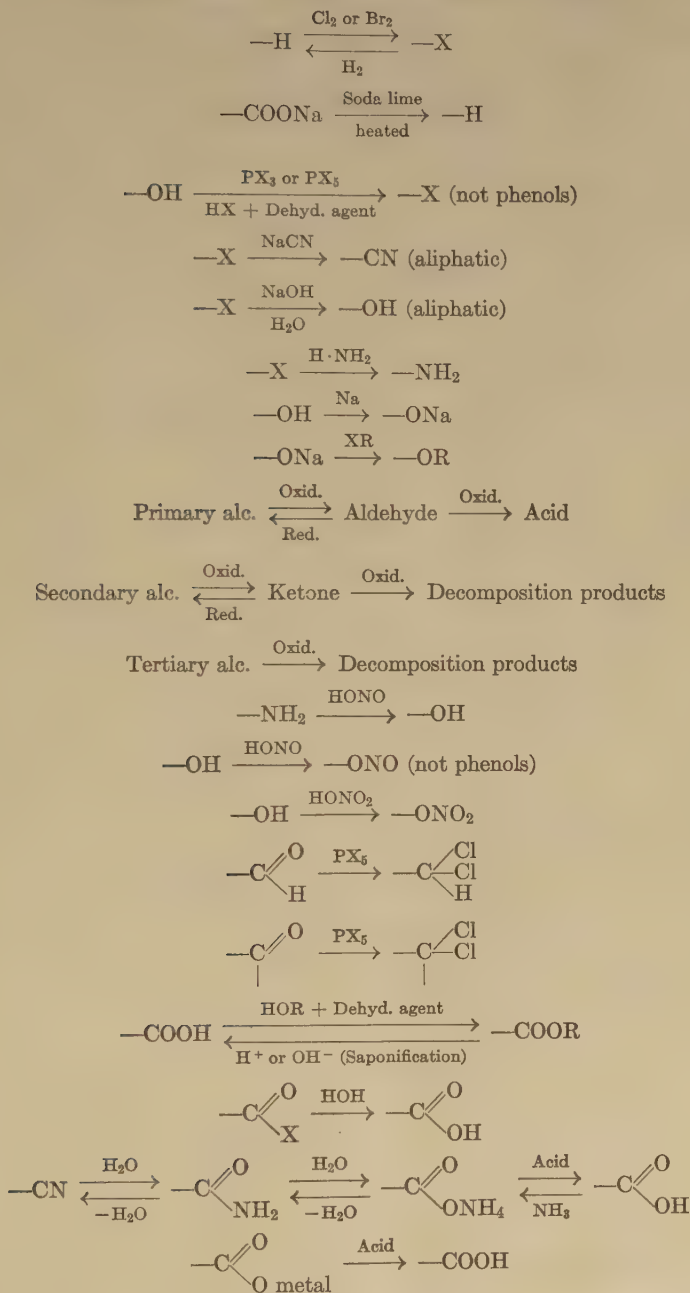
The presence of a sulfonic acid group increases the solubility of an organic compound in water.

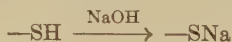
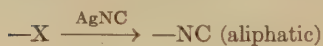
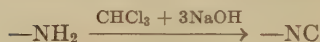
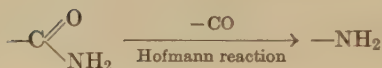
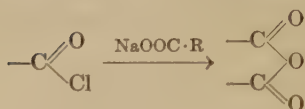
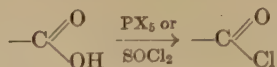
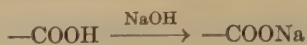
The hydroxy derivatives of aromatic hydrocarbons are soluble in water, but more so in alcohol and ether.

The *p*-compounds are, in general, less soluble in the various solvents than the isomeric *o*- and *m*-compounds.

Alkaloids are usually insoluble in water, but soluble in alcohol, chloroform, benzene, etc.

REPLACEMENT OF ELEMENTS AND GROUPS





ORGANIC TYPE FORMULAS

AROMATIC SERIES

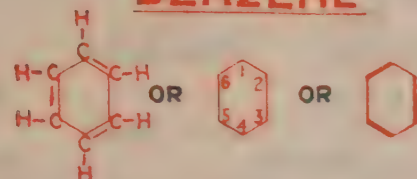
COLUMN I

COLUMN II

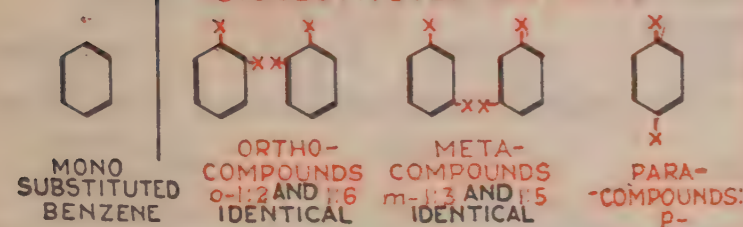
COLUMN III

COLUMN IV

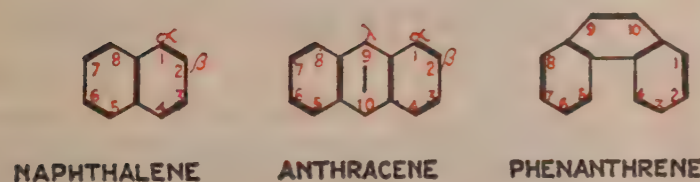
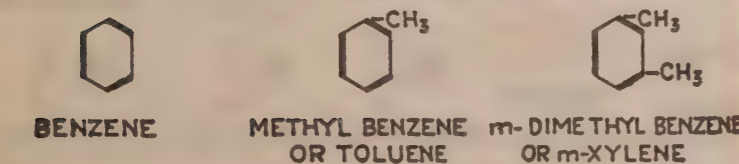
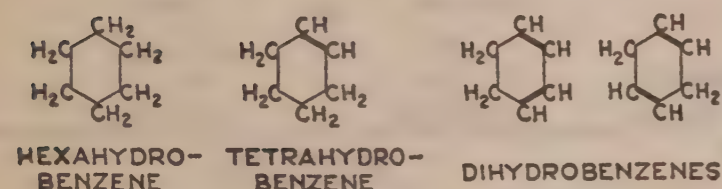
BENZENE



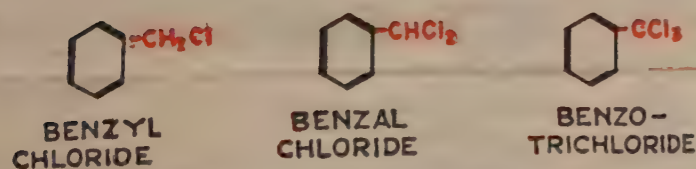
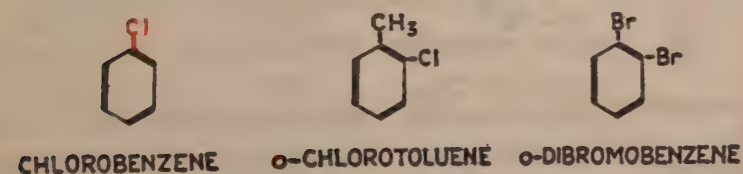
DISUBSTITUTED BENZENES



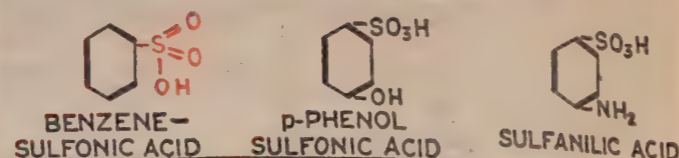
HYDROCARBONS



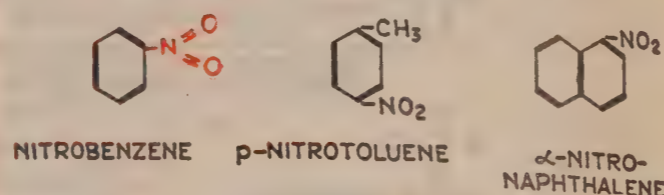
HALOGEN COMPOUNDS



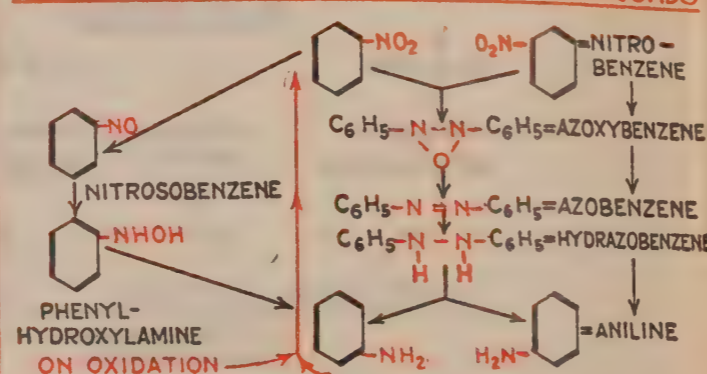
SULFONIC ACIDS



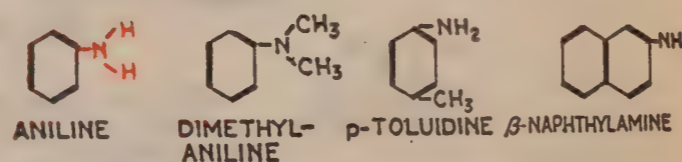
NITRO COMPOUNDS



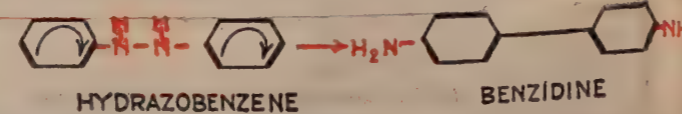
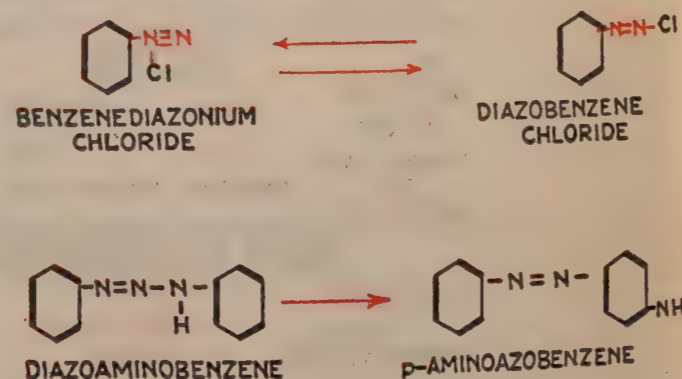
REDUCTION PRODUCTS OF NITRO-COMPOUNDS



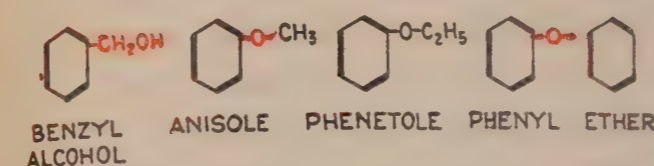
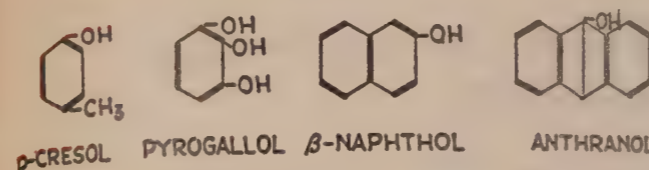
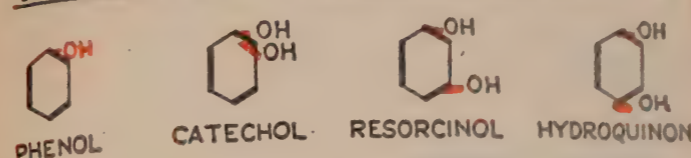
AMINO COMPOUNDS



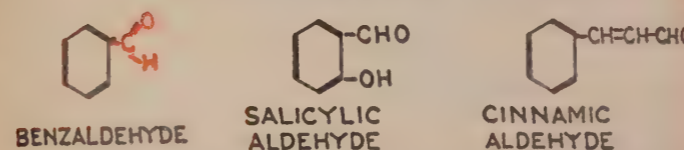
DIAZO AND AZO COMPOUNDS



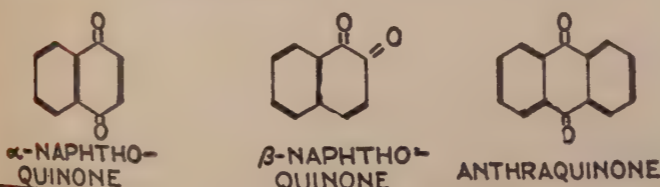
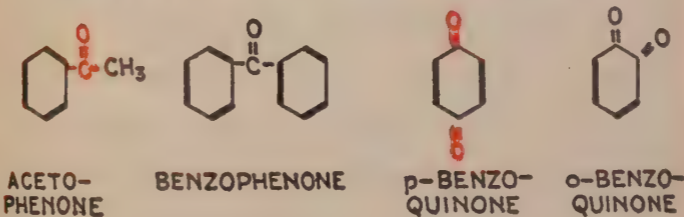
PHENOLS-ALCOHOLS-ETHERS



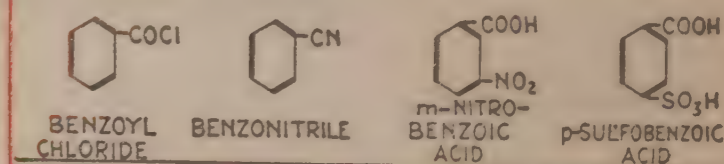
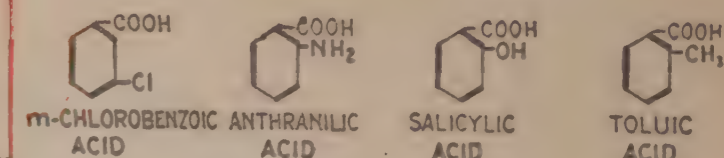
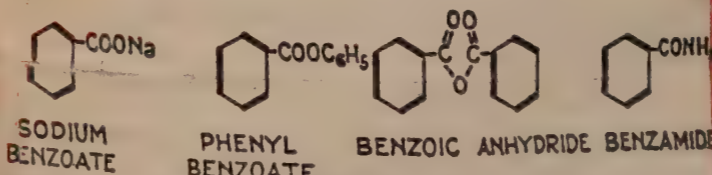
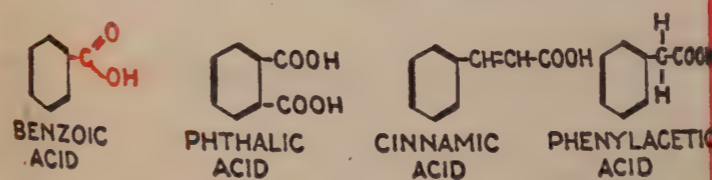
ALDEHYDES



KETONES AND QUINONES



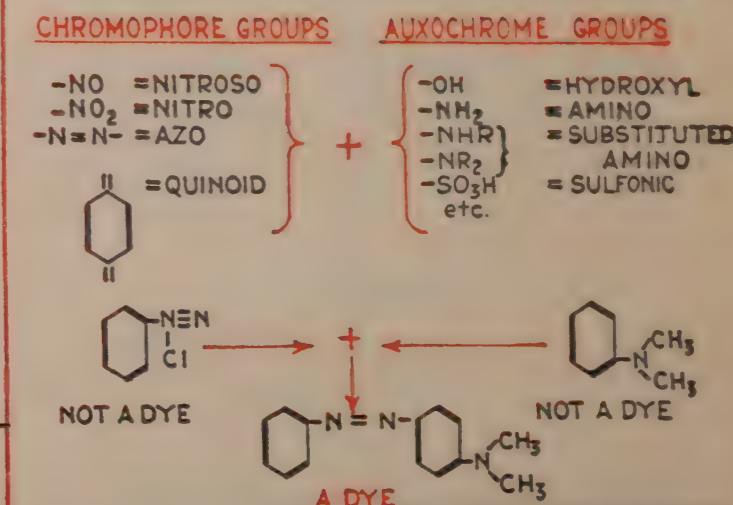
ACIDS AND RELATED COMPOUNDS



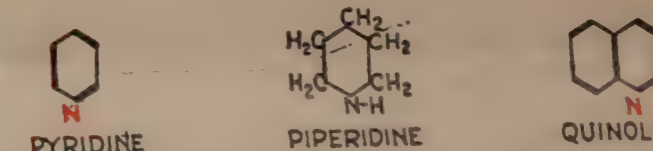
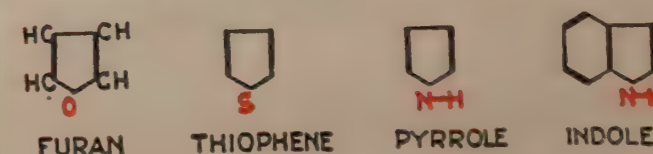
RULES FOR SUBSTITUTION

PRESENT IN POSITION I.	POSITION ENTERED BY SUBSTITUENTS					
	ALKYL	Cl	Br	I	NO ₂	SO ₃ H
ALKYL	4(2)	4(2)	4(2)	4(2)	4(2)(3)	4(2)(3)
Cl	4(2)	4(2)(3)	4(2)(3)	4	4(2)	4
Br	4(2)	4(2)(3)	4(2)(3)		4(2)	4
I		4	4	4	4(2)	4
OH	4(2)	4(2)	4(2)	4(2)	4(2)	4(2)
NH ₂	4(2)	4(2)	4	4	4(2)	4(2)
NO ₂	4(2)	3	3		3(2,4)	3(2,4)
SO ₃ H	4(2)		3		3(2,4)	3(4)
COOH	4(2)	3	3	3	3(2,4)	3(4)
CN			4		3	

CHARACTERISTIC GROUPS IN DYESTUFFS



HETEROCYCLIC COMPOUNDS



LIGHT LINES INDICATE SINGLE BONDS

HEAVY LINES INDICATE DOUBLE BONDS

Compiled by
ALEXANDER LOWY, Ph.D.
Professor of Organic Chemistry, University of Pittsburgh

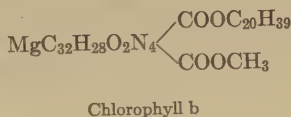
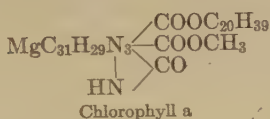
CHAPTER XXXV

PLANT AND ANIMAL PIGMENTS

CHLOROPHYLL, CAROTENE, XANTHOPHYLL, FLAVONES, ANTHOCYANINS, HEMOGLOBIN, AND BILE PIGMENTS

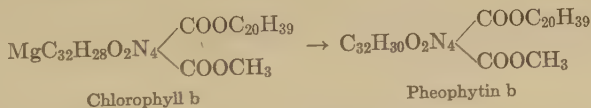
Chlorophyll. The chemistry of chlorophyll, the green pigment in plants, was worked out mainly by *Willstätter*, *Hans Fischer*, etc. Without going into any details, some of the essential points as to its structure and general characteristics may be given.

Chlorophyll is really a mixture of two substances:



Both contain the element magnesium in organic combination, and both are esters of a tribasic acid, chlorophyllin, combined with phytol, $\text{C}_{20}\text{H}_{39}\text{OH}$, and methanol.

With alkali the ester groups in chlorophyll are hydrolyzed, giving the corresponding carboxylic acids (chlorophyllins). The COOH groups can next be removed by heating with alkali. Acids (oxalic or HCl) remove the magnesium from the molecule; e.g.,



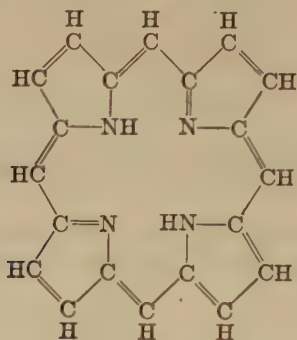
The oxidation of chlorophyll a or chlorophyll b yields, among other products, methyl ethyl maleinimide,

$$\begin{array}{c} \text{CH}_3 \cdot \text{C} - \text{CO} \\ \parallel \\ \text{C}_2\text{H}_5 \cdot \text{C} - \text{CO} \end{array} \text{NH}, \text{ and hematinic acid,}$$

$\text{HOOC} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{C} - \text{CO}$

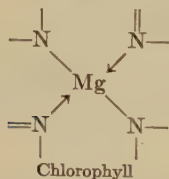
$$\begin{array}{c} \text{CH}_3 \cdot \text{C} - \text{CO} \\ \parallel \\ \text{C}_2\text{H}_5 \cdot \text{C} - \text{CO} \end{array} \text{NH}, \text{ products which are formed in the oxidation of hemoglobin.}$$

The fundamental nucleus of the natural pigments of the chlorophyll (plants) and hemin (p. 386, animals) groups is porphine,



Porphine

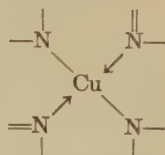
a combination of four pyrrole rings connected by methine, CH, groups. The stability of such a conjugate ring system is associated with a possible high degree of resonance. The metal atoms, Mg in chlorophyll and Fe in heme, are linked to the nitrogens by two covalences and two coordinate covalences (this may be considered double chelation):



Chlorophyll

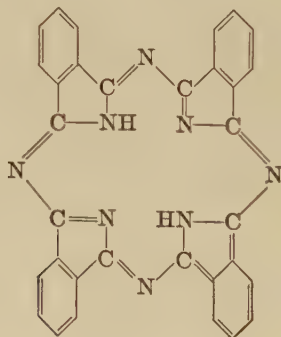


Heme



Phthalocyanine

Replacement of the four methine links by nitrogen yields the porphrazine structure, which, so far, is known only in the form of such synthetic derivatives as phthalocyanine



Phthalocyanine

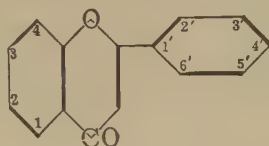
or tetrabenzoporphrazine. Metallic derivatives (for example, Cu) of this structure represent a recently developed family of stable, brilliant blue and green dyes, the *phthalocyanine* dyes.

In certain invertebrates like the crab, spider, and snail, *hemocyanin*, an organic copper complex, takes the place of the more usual hemoglobin.

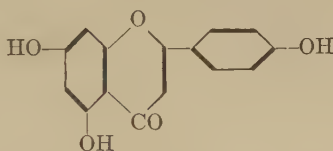
Carotene, which occurs in carrots, etc., is associated with chlorophyll in the green leaf. It is a hydrocarbon, $C_{40}H_{56}$. It is probably transformed in the body into vitamin A (p. 392).

Xanthophyll, also associated with chlorophyll (and carotene), has the formula $C_{40}H_{56}O_2$. It is assumed that both carotene and xanthophyll play an important role in plant respiration. (Pigments from the egg yolk and blood serum have been isolated which are identical with carotene and xanthophyll.)

Flavones. A number of yellow substances derived from flavone are found in plants



among them chrysin (1,3-dihydroxyflavone), which occurs in several varieties of poplar, and apigenin (1,3,4'-trihydroxyflavone),

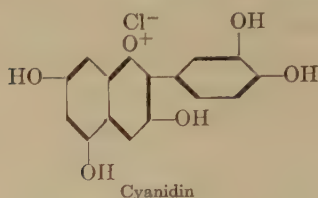


found in parsley and celery in the form of glucosides.

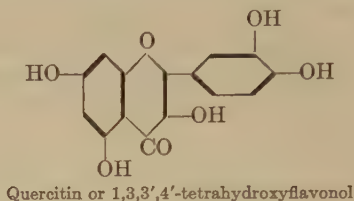
Anthocyanins are red, violet, and blue pigments present in flowers, fruits, leaves of plants, etc., in the form of glucosides. By hydrolysis, the anthocyanins are converted into glucose (or other monosaccharide) and **anthocyanidins**.

It is believed that these anthocyanins are reduction products of flavones (and, vice versa, that flavones are oxidation products of anthocyanins), and that changes from one to the other are brought about in the plant by oxidizing and reducing enzymes.

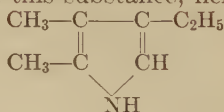
The anthocyanin in the cornflower and the rose is known as "cyanin," and this, on hydrolysis, yields two molecules of glucose and cyanidin (an anthocyanidin):



Willstätter also obtained this cyanidin by reducing quercetin, a hydroxy-flavone:



Hemoglobin, the red pigment in blood, is a combination of heme, an iron-containing substance, and globin, a protein belonging to the group of histones. It combines with oxygen and carbon monoxide, forming oxyhemoglobin and the more stable carboxyhemoglobin. "Hemin" (or "hematin chloride") is obtained from dried blood by boiling with glacial acetic acid. Very characteristic dark plates and prisms are obtained, which may be identified under the microscope. This reaction is used for the detection of blood. When hemoglobin is treated with H_2SO_4 , the iron is set free as ferrous sulfate, and hematoporphyrin, an iron-free porphyrin, results. From this substance, hemopyrrole,



may be obtained—a substance which is also a decomposition product of chlorophyll.

Closely related to hemoglobin in structure, in that they are iron pyrrole compounds, are several substances (enzymes, p. 389) found in minute quantities in various cells: cytochromes, catalase, and peroxidase. (Some of these enzymes—polyphenol oxidase, laccase, tyrosinase, ascorbic acid oxidase—are copper compounds.)

Bile pigments (bilirubin, biliverdin, bilicyanin, etc.) are the substances which are responsible for the characteristic color of bile. They are formed in the liver, originating from the hemoglobin of the blood. Bilirubin, $\text{C}_{32}\text{H}_{36}\text{N}_4\text{O}_6$, a reddish brown pigment found in abundance in Carnivora, is oxidized (even by the oxygen of the air) to biliverdin, $\text{C}_{32}\text{H}_{36}\text{N}_4\text{O}_8$, a green pigment, found largely in the bile of Herbivora.



JAMES BRYANT CONANT (1893-)

President of Harvard University. One of the outstanding organic chemists in America. He has made noteworthy contributions in the field of chlorophyll and hemoglobin chemistry and has contributed to a quantitative study of organic reactions. He has been awarded the Nichols medal.

Hydrobilirubin, a reduced product of bilirubin, is related to stercobilin, the pigment of the feces, and to urobilin, a pigment in urine. The *Gmelin* test for bile pigments—the play of colors obtained when concentrated HNO_3 is added to bile—is dependent upon the production of various colored oxidation products of the type of bilirubin and biliverdin.

Melanins. This group includes several different varieties of amorphous black or brown pigments which are insoluble in water, alcohol, ether, chloroform, and dilute acids, and which occur in skin, hair, etc. They are said to be derived from the amino acids tyrosine and tryptophan.

QUESTIONS

1. What is the characteristic inorganic element present in (a) chlorophyll; (b) hemoglobin? What fundamental structure do (a) and (b) have in common?
2. Which of the pigments in the green leaf is associated with a vitamin?
3. What is one chemical method for detecting blood?
4. What is the origin of the bile pigments?

CHAPTER XXXVI

ENZYMES, VITAMINS, HORMONES

ENZYMES

Enzymes are catalytic substances present in all living cells. They are responsible for many of the chemical changes which occur in the body. The word "enzyme" is from the Greek, meaning "in leaven," and is associated with the process of fermentation.

A number of the enzymes, such as pepsin and trypsin (both found in the digestive tract), have been isolated in the chemically pure state, and they turn out to be proteins, or proteins joined on to other groups. But their classification is still based on their "specificity"; that is to say, ptyalin, the enzyme found in saliva, will act on starch and one or two other carbohydrates, but not on proteins, whereas pepsin, the enzyme found in the gastric juice of the stomach, will act on proteins but not on carbohydrates.

Some of the better-known enzymes, together with their occurrence, the substances acted upon ("substrates"), and the products formed, are listed below. The ending *-ase* has been adopted to denote an enzyme; for example, sucrase is an enzyme, its name also suggesting that it acts on the sugar sucrose. However, old names like pepsin, trypsin, and rennin still remain.

1. *Esterases*.

(a) Pancreatic lipase, present in the pancreas, hydrolyzes fats into fatty acid and glycerol.

(b) Liver esterase, hydrolyzes esters of monohydric alcohols.

(c) Ricinus lipase, present in the castor bean, is similar to pancreatic lipase.

(d) Chlorophyllase, present in green plants, hydrolyzes chlorophyll, liberating phytol, $C_{20}H_{39}OH$.

(e) Phosphatases, present in several tissues, hydrolyze esters of phosphoric acid.

(f) Azolesterases, present in tissues, are enzymes which hydrolyze nitrogen-alcohol esters. An example is cholinesterase, which hydrolyzes acetylcholine, a substance related to choline.

2. *Proteinases and peptidases.*

(a) Pepsin, present in the stomach, hydrolyzes proteins to simpler products (peptones?).

(b) Trypsin, present in the pancreas, hydrolyzes proteins to simpler products (peptides and amino acids?).

(c) Rennin, sold as the "rennet" of commerce, present in the stomach, acts on casein to "clot" milk.

(d) Papain, found in the melon tree (papaw), etc., is probably similar to trypsin in its action.

(e) Bromelin, present in pineapple, is similar to papain.

(f) Cathepsin, found in liver and other animal cells, is similar to papain.

(g) Aminopolypeptidase, present in the intestine and usually acting in conjunction with trypsin, acts on polypeptides with a free amino group.

(h) Carboxypolypeptidase, present in the pancreas and usually acting in conjunction with trypsin, acts on polypeptides with a free carboxyl group.

(i) Dipeptidase, present in an impure enzyme in intestinal juice known as "erepsin," hydrolyzes dipeptides.

3. *Amidases.* (These act on carbon-nitrogen linkages.)

(a) Urease, present in leguminous plants (soybean and jack beans), converts urea into ammonia.

(b) Arginase, present in liver, converts arginine into ornithine and urea.

4. *Phosphorylases.*

Phosphorylases are enzymes which decompose polysaccharides and also bring about their synthesis. The formation (as well as the breakdown) of starch in plants and of glycogen in animals involves the action of these enzymes.

5. *Carbohydases.*

(a) Sucrase (saccharase, invertase), present in animal and plant tissues, hydrolyzes sucrose into glucose and fructose.

(b) Emulsin, present in bitter almonds, hydrolyzes the glucoside amygdalin into glucose, benzaldehyde, and hydrogen cyanide.

(c) Amylases, such as the ptyalin of saliva, found in animal and plant tissues, hydrolyze starch and glycogen into maltose.

6. *Oxidases.*

(a) Catalase, present in plant and animal tissues—e.g., liver—decomposes hydrogen peroxide into water and molecular oxygen.

(b) Dehydrogenases, found in many tissues—e.g., muscle—are enzymes which bring about oxidations by removal of hydrogen. For

example, succinic dehydrogenase converts succinic acid into fumaric acid.

(c) Peroxidases, present in many tissues—e.g., spleen and horse-radish—transfer peroxide oxygen to oxidizable substances.

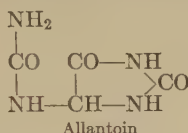
(d) Tyrosinase, present in the plant kingdom and in the tissues of invertebrates, converts tyrosine to a melanin-like (black) pigment.

(e) Laccase, present in bacteria, oxidizes polyphenols to quinones.

(f) Luciferase, present in fireflies, acts on luciferin to produce light.

(g) Indophenol oxidase, or cytochrome oxidase, present in various tissues, catalyzes the oxidation of a mixture of *p*-phenylenediamine and α -naphthol to indophenol; hence the name. This enzyme plays an important role in biological oxidations.

(h) Uricase, an enzyme found in liver and kidney, oxidizes uric acid to allantoin.



7. Zymase.

Zymase, present in yeast, converts glucose into alcohol and carbon dioxide.

Enzymes are soluble in water, dilute salt solutions, dilute alcohol, and glycerol. Like the proteins, they are precipitated by ammonium sulfate and concentrated alcohol. They are very easily adsorbed by various substances, and they show colloidal properties. They are, as a rule, destroyed at the temperature of boiling water; and their action is inhibited, but not destroyed, at 0° C. The enzymes act best (show an optimum activity) around 37–45° C.

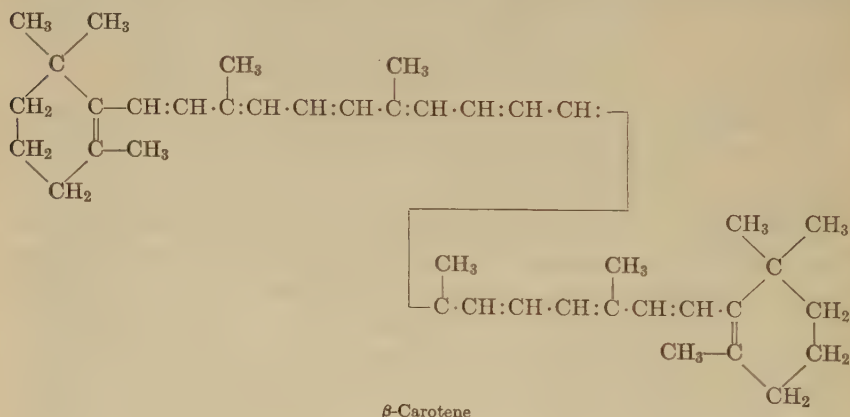
Enzymes are extremely susceptible to changes in hydrogen-ion concentrations, and for each enzyme there is a particular *pH* at which its reactivity is at a maximum (optimum reaction). For example, the optimum *pH* for trypsin is 8.0, that for pepsin 1.4, and for ptyalin 6.7. Thus, since the neutral point is *pH* 7, trypsin acts best in an alkaline solution, whereas pepsin acts best in a decidedly acid solution, and ptyalin is most reactive in a slightly acid medium.

VITAMINS

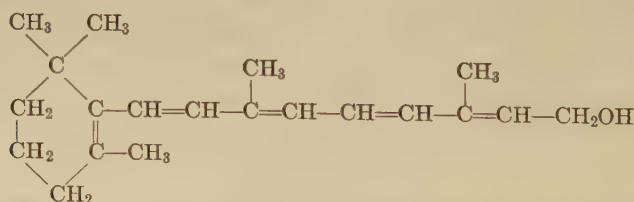
It has been found that, besides proteins, fats, carbohydrates, and mineral salts, there are other substances which, though needed in but minute quantities, are essential to life. These substances are known as *vitamins*. For purposes of identification, the vitamins are called A, B, C, D, E, and K. The presence of all is essential to well-being. As a

matter of fact, very few foods contain all of them. Milk is one of the rare exceptions, though the quantity of vitamin C which it contains is dangerously small. It is only by eating a variety of foods that we ensure ourselves a liberal allowance of all the vitamins.

Vitamin A is present in abundance in milk, butter, egg yolk, cod-liver oil, and, to a lesser extent, in beef fat and in many vegetable foods (lettuce, spinach, cabbage, carrots, potatoes, etc.). Lard and vegetable oils, such as olive oil, are practically devoid of it. Cereals (wheat, rye, barley, etc.) contain little. In a general way, the statement may be made that this vitamin is present in green leaves and in the embryos of many seeds. Carotene, $C_{40}H_{56}$, has been shown to be transformed into vitamin A in the liver. Carotene can, in fact, be used in place of vitamin A in the diet; it is found, together with a number of other modified carotenes, in green leaves, carrot roots, etc. Carotene has several isomeric forms:



Vitamin A is believed to have the formula $C_{20}H_{30}O$. It consists of a β -ionone ring attached to isoprene residues. It is probably formed from carotene by the rupture and hydration of the central ethylene bond, giving



The absence of vitamin A in the diet gives rise to an eye disease known as *xerophthalmia*. The earlier stage of the disease may show itself in night blindness, which is due to a deficiency of the pigment in the

retina known as *visual purple*. As the vitamin A is increased, the visual purple increases correspondingly.

There is evidence for two vitamins A, each one having a specific absorption spectrum band.

Vitamin B, present in yeast, liver, and various grains, etc., in reality consists of several vitamins. They can now be classified as follows:

1. *Thiamin*, vitamin B₁, antineuritic factor, aneurine. This is easily destroyed by heat. It prevents and cures beriberi in man and a corresponding disease in birds known as polyneuritis.

2. *Riboflavin*, vitamin B₂, vitamin G, a growth factor.

3. *Niacin* or nicotinic acid, and nicotinic acid amide, P-P (pellagra-preventive) factor.

4. *Pyridoxine*, vitamin B₆, antidermatitis factor.

5. *Panthothenic acid*, filtrate factor, chick antidermatitis factor.

6. *Biotin*, vitamin H, coenzyme R, anti-egg white injury factor, needed for the growth of yeasts, molds, and bacteria.

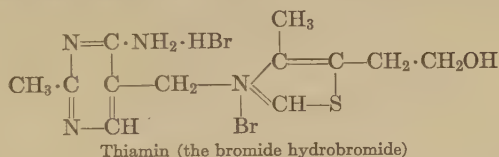
7. *p-Aminobenzoic acid*, a possible anti-gray hair factor.

8. *Inositol*, mouse anti-alopecia¹ factor, promotes growth in the chick and cures "spectacle eyes" in rats.

9. *Choline*, a growth factor, also prevents perosis² in chicks. Its methyl groups are utilized by the body for methylating compounds.

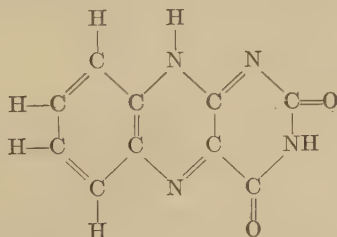
10. *Folic acid*, a growth factor for chicks (?) and bacteria.

Thiamin has been isolated and synthesized. Its constitution is



the first part of the molecule showing a pyrimidine grouping, and the second part a thiazole grouping.

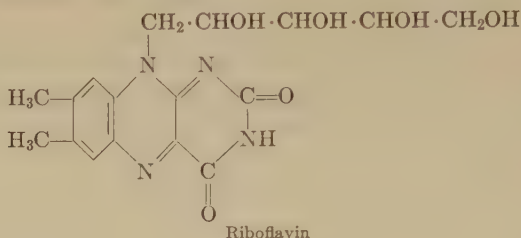
Riboflavin, also isolated and synthesized, is a derivative of isoalloxazine,



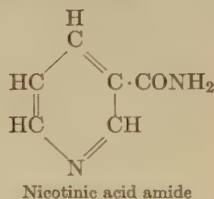
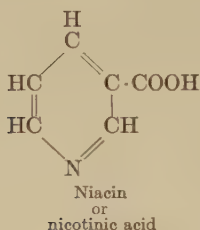
¹ Alopecia means baldness.

² Perosis means a shortening and thickening of the bones.

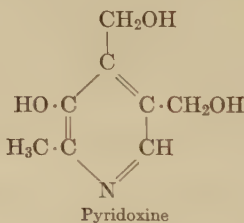
When the derivative of isoalloxazine is attached to ribitol, a five-carbon sugar alcohol, riboflavin¹ results:



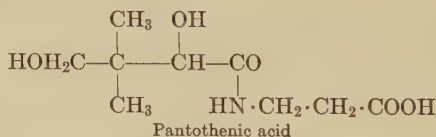
Niacin and its amide have the following formulas:



Pyridoxine, which has also been isolated and synthesized, is, like nicotinic acid, a pyridine derivative:

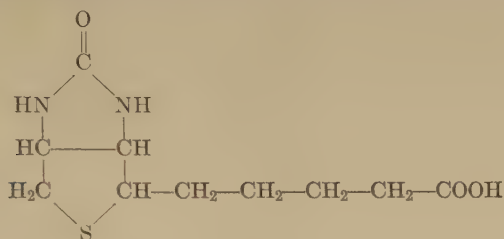


Pantothenic acid is a condensation of β -alanine and a methylated derivative of butyric acid:



¹One or two of the oxidases are structurally related to riboflavin, a fact which suggests a possible reason for the need of riboflavin by the body.

Biotin is a condensation of two rings: the imidazole and the thiophene rings. The side chain is valeric acid:

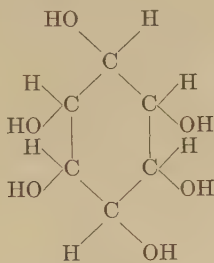


Biotin

p-Aminobenzoic acid is, of course,

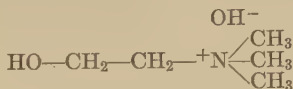
*p*-Aminobenzoic acid

Inositol is hexahydroxycyclohexane:



Inositol

Choline has already been referred to (p. 127):



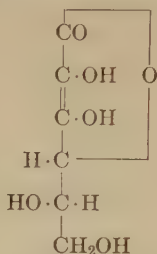
Choline

Little is known about the structure of folic acid.

Ascorbic Acid, Vitamin C, Cevitamic Acid. Most fresh fruits and fresh vegetables contain vitamin C. The emphasis is advisedly put on fresh material. The orange and the tomato are particularly good sources.

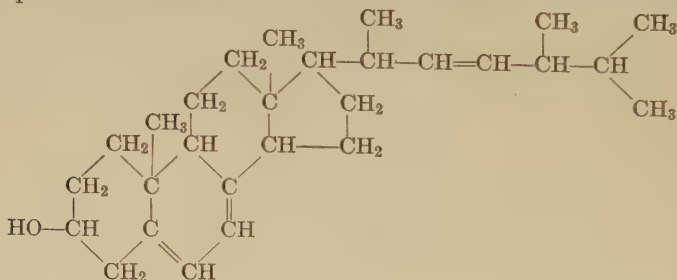
Ascorbic acid has been isolated in chemically pure form and its consti-

tution determined. It is a derivative of *l*-gulose, an isomer of glucose. Its formula (in the lactone form) is:



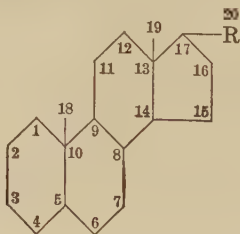
Vitamin D is present in greatest abundance in halibut- and cod-liver oils, in egg yolk (much less), and in milk (much smaller quantity). It is produced when some foods are irradiated with ultraviolet light. One vitamin D is synthesized when ergosterol is irradiated. Another vitamin D probably has its origin in cholesterol. The function of vitamin D is to aid in the proper utilization of calcium and phosphorus. It takes part in tooth and bone formation.

Ergosterol, $\text{C}_{28}\text{H}_{44}\text{O}$, is structurally related to cholesterol (p. 397) and has the probable formula:



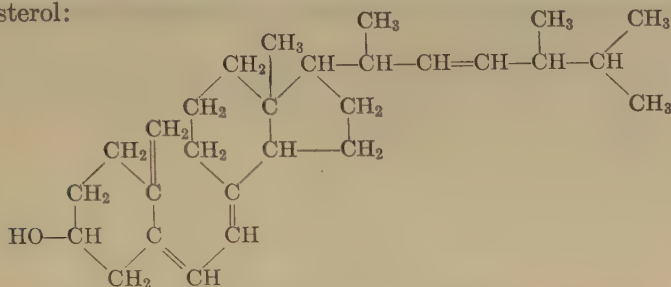
which makes the compound a partially hydrogenated phenanthrene derivative.

As a matter of fact, the characteristic structure common to several groups of natural products (among them sterols and sex hormones) is *cyclopentanoperhydrophenanthrene*.



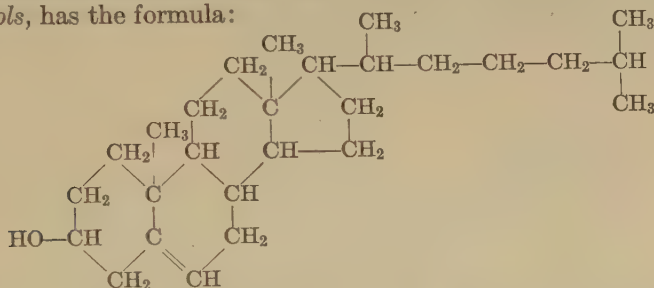
A cyclopentanoperhydrophenanthrene derivative

It is believed that the conversion of ergosterol into a vitamin D—is due to the opening up of the second ring in ergosterol:

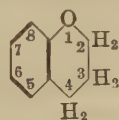


A vitamin D (sometimes called "calciferol")

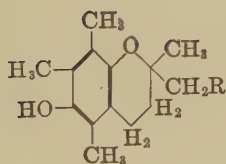
Cholesterol, $C_{27}H_{46}O$, which has already been referred to (p. 128), and which, like ergosterol, belongs to a group of compounds known as the *sterols*, has the formula:



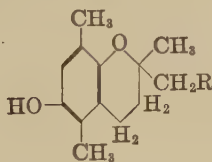
Vitamin E, the antisterility vitamin, is also known as **tocopherol** (from the Greek, *tokos*—childbirth; *phero*—I bear). Three isomeric tocopherols are known, and all are derivatives of chromane:



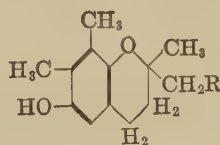
Chromane



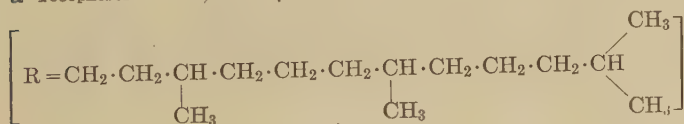
α -Tocopherol



β -Tocopherol



γ -Tocopherol

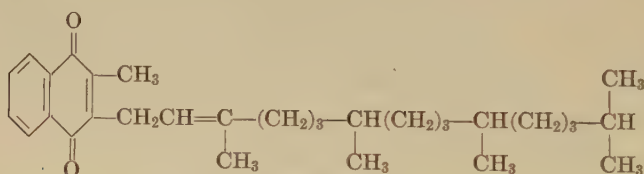


Vitamin K is a vitamin the absence of which gives rise to a hemorrhagic disease in chicks. The disease is associated with a decrease in the amount of prothrombin in the blood—a substance necessary for the formation of the blood clot.

Vitamin K is widely distributed: in alfalfa, spinach, tomatoes, liver, several bacteria, etc. It has been isolated and its structure established. It is a derivative of 1,4-naphthoquinone:



and here the side chain attached to this compound turns out to be a phytyl radical.



Vitamin K

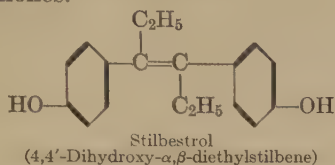
There are two vitamins K, the second one having a different side chain.

HORMONES

In the body there are various ductless glands (glands without tubes), such as the thyroid, the pituitary, the adrenals, etc., which manufacture specific substances that find their way into the blood stream and influence other organs of the body. The substances so manufactured are called "hormones" (from the Greek "to excite") or "chemical messengers." These hormones profoundly influence various activities of the body. Several hormones have been isolated in the pure condition.

Epinephrine or Adrenaline. One of the hormones of the adrenal glands may be isolated by first treating concentrated adrenal extracts with alcohol, lead acetate, etc.; then precipitating the active substance by the addition of concentrated ammonia. The precipitate is purified by repeatedly dissolving in acid and reprecipitating with ammonia. The adrenaline may be synthesized by the following reactions:

stilbestrol, is physiologically even more potent than some of the naturally occurring female hormones.



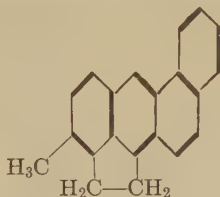
It has also been shown that the bile acids, essential constituents of the bile, and certain plant glucosides (from digitoxin, for example) have structures similar to those of the sterols.

Cancer-producing substances (in mice) have been prepared synthetically which have similar basic groupings. Among them may be mentioned those belonging to the dibenzanthracene type:

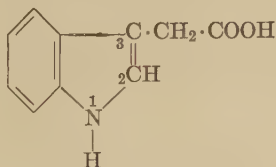


which may be looked upon as condensed phenanthrene rings.

Another powerful cancer-producing substance is methylcholanthrene:



Hormones obtained from the tips of oat and corn stems have been shown to play a part in *plant* development. These are **plant hormones**. Two of them (*auxins*) have been isolated; they are complicated hydroxy acids. A number of relatively simple chemical substances have also been shown to have growth-promoting activity. One of these substances is indole-3-acetic acid:



QUESTIONS

1. Compare enzymes with catalysts.
2. What is the probable chemical composition of some of these enzymes?
3. What are some of the substances present in the vitamin B complex?
4. (a) What is the vitamin present in most fruits and vegetables? (b) To what group of chemical substances is this vitamin related?
5. What compound may be regarded as the mother substance of one of the vitamins D?
6. Give an example of a sterol.
7. Give the structural formulas of (a) adrenaline; (b) thyroxine.

CHAPTER XXXVII

NOMENCLATURE OF ORGANIC COMPOUNDS

The number of organic compounds is in excess of 250,000, and the naming of such compounds presents no little difficulty. Some of the methods of naming organic compounds have been explained throughout the book. In the present chapter, the methods adopted will be briefly summarized. In addition, the naming of various groups, and the principles involved in the naming of a number of somewhat complex compounds, will be discussed. It is hoped that such an outline will prove of value to the student of chemistry who is about to begin more advanced work in organic chemistry, or in one of its many applications, and who will have occasion to consult the standard reference books and the current literature.

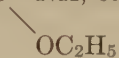
It would be well, at the outset, for the student to review the chart of type formulas between pages 382 and 383. From this chart, as well as from our study, we may deduce the following rules:

A word ending in	Indicates
-ane	paraffin
-ene or -ylene	olefin
-yne	acetylene
-diene	diolefin
-diyne	diacetylene
-ene	aromatic hydrocarbon (as a rule)
-in	glycerides, glucosides, proteins, some enzymes
-ine	alkaloids, amines
-ol	hydroxyl group (alcohol or phenol)
-diol	two hydroxyl groups
-al	aldehyde
-one	ketone (or quinone)
-ic (sometimes -oic)	acid
-ase	enzyme
-ose	sugars
-ate, -ite	salt, ester

In naming ¹ a compound so as to indicate that oxygen is replaced by sulfur, the prefix *thio* is used; e.g., HCNS, *thiocyanic acid*; CS(NH₂)₂, *thiourea*.

¹ These suggestions are taken from the publications of the American Chemical Society

The names of the groups NH_2 , NHR , NR_2 , NH , or NR end in *-ido* only when they are substituents in an acid group, otherwise in *-ino*; e.g., $\text{CH}_3 \cdot \text{C}=\text{NH}$, ethyl imidoacetate; $\text{CH}_2 \cdot \text{CH}_2 \cdot \text{COOH}$, β -aminopropionic



acid.

Salts of organic bases with hydrochloric acid are called *hydrochlorides*; e.g., $\text{C}_6\text{H}_5 \cdot \text{NH}_2 \cdot \text{HCl}$, aniline *hydrochloride*, or $\text{C}_6\text{H}_5\text{NH}_3\text{Cl}$, anilinium chloride.

Compounds which are not alcohols, but have received names ending in *-ol*, are spelled *-ole*, as anisole, indole. C_6H_6 is called *benzene* (not benzol), C_7H_8 *toluene*, etc.

The endings *-ine* are used for basic substances, and *-in* for glycerides, glucosides, bitter principles, proteins, etc.; e.g., aniline, purine, morphine; but *gelatin*, *palmitin*, *amygdalin*, *albumin*, *protein*.

In naming organic compounds the connective *o* is used in such names of substituent radicals as *amino-*, *bromo-*, *cyano-*, and *iodo-*; e.g., bromobenzene, chloroacetic acid, nitroaniline.

Acid radicals, such as $\text{C}_6\text{H}_5\text{CO}$, end in *-yl*, and their compounds with halogens, as $\text{C}_6\text{H}_5\text{COCl}$, are called *chlorides*, *bromides*, etc.; e.g., benzoyl chloride.

The names butane, pentane, etc., are used only for the normal hydrocarbons, with the prefix *cyclo-*, for saturated cyclic hydrocarbons.

To designate ortho-, meta-, para-, dextro-, levo-, racemic, symmetrical, secondary, tertiary, and meso, use *o-*, *m-*, *p-*, *d-*, *l-*, *dl-*, *sym-*, *sec-*, *tert-*, and *meso-*, respectively.

Me, *Et*, *Ph*, etc., are abbreviations sometimes used for methyl, ethyl, phenyl, etc., groups.

Numerals precede the part of the name to which they refer; e.g., 2-bromo-3-methylbenzenesulfonic acid.

The following list gives the names of a number of important organic radicals: ¹

¹ The list is taken from Chemical Abstracts, *Third Decennial Index*, May 1, 1938.

acenaphthenyl $C_{12}H_8$ —(from *acenaphthene*)

acetamido CH_3CONH —

acetylenyl = ethynyl

acetimido $CH_3C(:NH)$ —

acetonyl CH_3COCH_2 —

acetonylidene $CH_3COCH=$

acetoxy CH_3COO —

acetyl CH_3CO —

acetylene $=CHCH=$

acridyl $C_{13}H_9N$ —(from *acridine*)

acrylyl $CH_2=CHCO$ —

adipyl $-OC(CH_2)_4CO-$

alanyl CH_3CHNH_2CO-

alkoxy RO —(R = any alkyl radical)

allyl $CH_2=CHCH_2$ —

β -allyl = isopropenyl

amidoxalyl = oxamyl

amino (amido) H_2N —

amoxy $CH_3(CH_2)_4O$ —

amyl $CH_3(CH_2)_4$ —

tert-amyl

amylidene $CH_3(CH_2)_3CH=$

anilino C_6H_5NH —

anisal = anisylidene

anisoyl $p-CH_3OC_6H_4CO-$

anisyl = methoxyphenyl

anisylidene $p-CH_3OC_6H_4CH=$

anthranoyl $o-H_2NC_6H_4CO-$

anthraquinonyl $C_{14}H_9O_2$ —(from *anthraquinone*,

2 isomers)

anthryl $C_{14}H_9$ —(from *anthracene*, 3 isomers)

anthrylene $-C_{14}H_8-$ —(from *anthracene*, 14 isomers)

antimono $-Sb:Sb-$

antipyril (from *antipyrine*)

$OC \cdot N(C_6H_5) \cdot N(CH_3) \cdot C(CH_3) \cdot C-$

arseno $-As:As-$

arsosio $O:As-$

arsinico (from *arsinic acid*) $(HO)OAs=$

arsino H_2As-

arso O_2As-

arsono (from *arsonic acid*) $(HO)_2OAs-$

arsylene $HAs=$

asaryl 2,4,5- $(CH_3O)_3C_6H_2$ —

asparagyl $H_2NCOCH_2CHNH_2CO-$

aspartyl $-COCH_2CHNH_2CO-$

auro $Au-$

azido = triazo

azino = $NN=$

azo $-N:N-$

azoxy $-N(O)N-$

benzal = benzylidene

benzamido C_6H_5CONH-

benzenyl = benzylidene

benzidino $H_2NC_6H_4C_6H_4NH-$ —(from *benzidine*)

benziloyl $(C_6H_5)_2C(OH)CO-$

benzimidazolyl $C_7H_5N_2$ —(from *benzimidazole*)

benzimido $C_6H_5C(:NH)-$

benzofuryl C_8H_6O —(from *benzofuran*)

benzohydryl $(C_6H_5)_2CH-$

benzohydrylidene $(C_6H_5)_2C=$

benzopyranyl C_9H_7O —(2- α , etc.) (from *benzopyran*)

benzoxazolyl C_7H_4NO —(from *benzoxazole*)

benzoxy C_6H_5COO-

benzoyl C_6H_5CO-

benzoylene $-C_6H_4CO-$

benzyl $C_6H_5CH_2$ —

benzylidene $C_6H_5CH=$

benzylidene $C_6H_5C=$

biphenylene $-C_6H_4C_6H_4-$

biphenylenedisazo $-N:N-C_6H_4C_6H_4N:N-$

biphenyl (2-, 3- or 4-) $C_6H_5C_6H_4$ —(from *bi-*

phenyl)

bornyl (from *borneol*)

$CH_2 \cdot CH \cdot CH_2 \cdot CH_2 \cdot C(CH_3) \cdot CH-$

3 4 5 6 1 2

boryl $O:B-$

bromo $Br-$

1-butenyl $CH_3CH_2CH:CH-$

2-butenyl $CH_3CH:CHCH_2-$

3-butenyl $CH_2=CH(CH_2)_2-$

butoxy $CH_3(CH_2)_3O-$

butyl $CH_3(CH_2)_3-$

sec-butyl

$CH_3CH_2 \begin{matrix} \diagup \\ CH- \end{matrix}$

CH_3

tert-butyl $(CH_3)_3C-$

butylene (1,4) = tetramethylene

butylidene $CH_3(CH_2)_2CH=$

butyryl $CH_3(CH_2)_2CO-$

camphanyl $C_{10}H_{17}$ —(from *camphane*, 3 isomers)

camphoroyl $C_{10}H_{14}O_2$ —(from *camphoric acid*)

camphoryl $C_{10}H_{16}O$ —(from *camphor*)

camphorylidene $C_{10}H_{14}O=$ —(from *camphor*)

caproyl $CH_3(CH_2)_4CO-$

capryl $CH_3(CH_2)_5CO-$

caprylyl $CH_3(CH_2)_5CO-$

carbamido = ureido

carbamyl H_2NCO-

carbanilino = phenylcarbamyl

carbazolyl $C_{12}H_9N$ —(from *carbazole*, 5 isomers)

carbethoxy C_2H_5OOC-

carbomethoxy CH_3OOC-

carbonyl $OC=$

carbonyldioxy $-OCOO-$

carboxy $HOOC-$

carbyl $-C-$

carvaeryl (4) $(CH_3)_2CH \begin{matrix} \diagup \\ C_6H_5- \end{matrix}$ (2)

cetyl $CH_3(CH_2)_{14}CH_2-$

chloro $Cl-$

chloromercuri $ClHg-$

cinnamal = cinnamylidene

cinnameryl = styryl

cinnamoyl $C_6H_5CH:CHCO-$

cinnamyl $C_6H_5CH_2CH:CH-$

cinnamylidene $C_6H_5CH:CHCH=$

cresotyl 2,3- $HO(CH_3)C_6H_3CO-$ —(from *cresotic acid*) (2, 3-shown)

cresoxy = toloxy

cresyl = *ar*-hydroxytolyl; = tolyl

cresylene = tolylene

crotonyl $CH_3CH:CHCO-$

cumal = cumylidene

cumenyl $(CH_3)_2CHC_6H_4-$

cumidino $(CH_3)_2CHC_6H_4NH-$

cuminal = cumylidene

cumoyl (from *cumic acid*) $p-(CH_3)_2CHC_6H_4CO-$

cumyl $p-(CH_3)_2CHC_6H_4CH_2-$

cumylidene $p-(CH_3)_2CHC_6H_4CH=$

cycano $NC-$

cyclobutyl (from *cyclobutane*) C_4H_7-

cyclohexadienyl (2,4- shown)

$CH_2 \cdot CH:CH \cdot CH:CH-$

6 5 4 3 2 1

cyclohexadienylidene (2,4- or 2,5-; 2,5- shown)

$CH:CH \cdot CH_2 \cdot CH:CH \cdot C=$

cyclohexenyl C_6H_9 —(from *cyclohexene*, 3 isomers)

cyclohexenylidene (2-shown)

$CH_2 \cdot CH_2 \cdot CH_2 \cdot CH:CH \cdot C=$

cyclohexyl C_6H_{11} —(from *cyclohexane*)

cyclohexylidene $CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot C=$

cyclopentenyl C_5H_7 —(from *cyclopentene*)

cyclopentyl C_5H_9 —(from *cyclopentane*)

cyclopropyl C_3H_5 —(from *cyclopropane*)

cymyl $C_{10}H_{13}$ —(from *cymene*)

2-*p*-cymyl = carvaeryl

3-*p*-cymyl = thymyl

desyl $C_6H_5COCH(C_6H_5)-$

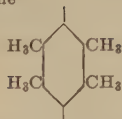
diazoo $-N:N-$

diazamino $-N:NNH-$

dodecyl $CH_3(CH_2)_{10}CH_2-$

duryl 2,3,5,6- $(CH_3)_4C_6H-$

durylene



epoxy—O—(to different atoms already united in some other way)

ethene = ethylene

ethenyl = ethylidene; = vinyl

ethinyl = ethynyl

ethoxalyl $\text{C}_2\text{H}_5\text{OCCO}$ —ethoxy $\text{C}_2\text{H}_5\text{O}$ —ethyl CH_3CH_2 —ethylene— CH_2CH_2 —ethylenedioxy— $\text{O}(\text{CH}_2)_2\text{O}$ —ethylidene $\text{CH}_3\text{CH}=\text{}$ ethylidene $\text{CH}_3\text{C}=\text{}$ ethynyl $\text{CH}:\text{C}$ —ethynylene— $\text{C}:\text{C}$ —fenchanyl $\text{C}_{10}\text{H}_{17}$ —(from fenchane)fenchyl $\text{C}_{10}\text{H}_{17}$ —(= 2-fenchanyl)fluorenyl C_{13}H_9 —(from fluorene, 5 isomers)fluorenylidene $\text{C}_{13}\text{H}_8=\text{}$

fluoro F—

formamido HCONH —

formazyl

formyl $\text{OCH}=\text{}$

furfural = furfurylidene

furfuryl $\text{O}:\text{CH}:\text{CH}:\text{CH}:\text{CCH}_2$ —

furfurylidene (2 isomers, 2-shown)

2-furoyl $\text{O}:\text{CH}:\text{CH}:\text{CH}:\text{CCO}$ —3-furoyl $\text{CH}:\text{CH}:\text{O}:\text{CH}:\text{CCO}$ —furyl (2 isomers, 2-shown) $\text{O}:\text{CH}:\text{CH}:\text{CH}:\text{C}$ —

furylidene

geranyl $\text{C}_{10}\text{H}_{17}$ —(from geraniol)glutamyl— $\text{OCCHNH}_2(\text{CH}_2)_2\text{CO}$ —glutaryl— $\text{OC}(\text{CH}_2)_3\text{CO}$ —glyceryl— CH_2CHCH_2 —glycolyl HOCH_2CO —glycyl $\text{H}_2\text{NCH}_2\text{CO}$ —glyoxylyl OCHCO —

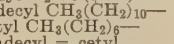
guaiacyl = o-methoxyphenyl

guanido $\text{H}_2\text{NC}:(\text{NH})\text{NH}$ —guanyl $\text{H}_2\text{NC}:(\text{NH})$ —hendecyl $\text{CH}_3(\text{CH}_2)_{10}$ —heptyl $\text{CH}_3(\text{CH}_2)_6$ —

hexadecyl = cetyl

hexyl $\text{CH}_3(\text{CH}_2)_5$ —hippuryl $\text{C}_6\text{H}_5\text{CONHCH}_2\text{CO}$ —homopiperonyl 3,4-(CH_2O_2) $\text{C}_6\text{H}_3\text{CH}_2\text{CH}_2$ —

hydrazo



(to same atom)

hydrazino H_2NNH —hydrazo— HNNH —(to different atoms)hydrazono $\text{H}_2\text{NN}=\text{}$ hydroxamino HONH —

hydroximino = isonitroso

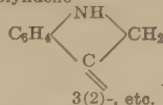
hydroxy (hydroxyl) HO —

-idene added to any radical usually means a

double bond at point of attachment

imidazolyl $\text{C}_3\text{H}_3\text{N}_2$ —(from imidazole, 4 isomers)imino (imido) $\text{NH}=\text{}$ indanyl C_9H_9 —(from indan, 4 isomers)indenyl C_9H_7 —(from indene, 7 isomers)indolyl $\text{C}_8\text{H}_7\text{N}$ —(from indole, 7 isomers)

indolylidene



3(2)-, etc.

indyl = indolyl

iodo I—

iodoso OI —iodoxyl O_2I —

isoallyl = propenyl

isoamoxy $(\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{O}$ —isoamyl $(\text{CH}_3)_2\text{CHCH}_2\text{CH}_2$ —isoamylidene $(\text{CH}_3)_2\text{CHCH}_2\text{CH}=\text{}$

isobutenyl = 2-methylpropenyl

isobutoxy $(\text{CH}_3)_2\text{CHCH}_2\text{O}$ —isobutyl $(\text{CH}_3)_2\text{CHCH}_2$ —isobutyryl $(\text{CH}_3)_2\text{CHCO}$ —isocyanato $\text{C}:\text{N}$ —isohexyl $(\text{CH}_3)_2\text{CH}(\text{CH}_2)_3$ —isoindolyl $\text{C}_8\text{H}_7\text{N}$ —(from isoindole, 4 isomers)isoleucyl $\text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3)\text{CHNH}_2\text{CO}$ —isonitro $\text{HOON}=\text{}$ isonitroso $\text{HON}=\text{}$

1-isopentenyl = 3-methyl-1-butenyl

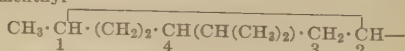
isophthalal = isophthalylidene

isophthaloyl— $\text{OCC}_6\text{H}_4\text{CO}$ —(m)isophthalylidene— $\text{HCC}_6\text{H}_4\text{CH}=\text{}$ (m)isopropenyl $\text{CH}_2:\text{C}(\text{CH}_3)=$ isopropoxy $(\text{CH}_3)_2\text{CHO}$ —isopropyl $(\text{CH}_3)_2\text{CH}$ —isopropylidene $(\text{CH}_3)_2\text{C}=\text{}$ isoquinolyl $\text{C}_9\text{H}_6\text{N}$ —(from isoquinoline, 9 isomers)isothiocyano $\text{S}:\text{C}:\text{N}$ —isovaleryl $(\text{CH}_3)_2\text{CHCH}_2\text{CO}$ —isozalyl $\text{C}_8\text{H}_2\text{NO}$ —(from isoxazole, 5 isomers)

keto = oxo

lauryl (from lauric acid) $\text{CH}_3(\text{CH}_2)_{10}\text{CO}$ —leucyl (from leucine) $(\text{CH}_3)_2\text{CHCH}_2\text{CHNH}_2\text{CO}$ —malonyl— OCCH_2CO —

methyl



(from menthane)

mercapto HS—

mercuri—Hg—

 α -mesityl 3, 5-(CH_3) $_2\text{C}_6\text{H}_3\text{CH}_2$ —2-mesityl 2, 4, 6-(CH_3) $_3\text{C}_6\text{H}_2$ —

methene = methylene

methenyl = methylidene

methionyl $\text{CH}_2(\text{SO}_2)_2=\text{}$ methoxy CH_3O —methyl CH_3 —methylene $\text{CH}_2=\text{}$ methylenedioxy— OCH_2O —methylidene $\text{CH}=\text{}$

methylol = (hydroxymethyl)

myristoyl (from myristic acid) $\text{CH}_3(\text{CH}_2)_{12}\text{CO}$ —

naphthal = naphthylmethylene

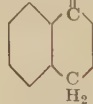
naphthalimido (from naphthalic acid)

 $\text{C}_{10}\text{H}_6(\text{CO})_2\text{N}$ —

naphthenyl = naphthylmethylidene

naphthoxy $\text{C}_{10}\text{H}_7\text{O}$ —naphthoyl $\text{C}_{10}\text{H}_7\text{CO}$ —naphthyl (1- or 2-) C_{10}H_7 —naphthylene $\text{C}_{10}\text{H}_6=\text{}$

naphthylidene



1(4)-, etc.

nitramino O_2NNH —

nitrilo $\text{N}\equiv$
 nitro $\text{O}_2\text{N}-$
aci-nitro = isonitro
 nitroso $\text{ON}-$
 norcamphanyl $\text{C}_7\text{H}_{11}-$ (from *norcamphane*)
 octyl $\text{CH}_3(\text{CH}_2)_7-$
 oleoyl (from *oleic acid*) $\text{C}_{17}\text{H}_{33}\text{CO}-$
 oxalyl $-\text{OCCO}-$
 oxamido $\text{H}_2\text{NCOCONH}-$
 oxamyl $\text{H}_2\text{NCCOCO}-$
 oximido = isonitroso
 oxo $\text{O}=(\text{to same atom})$
 oxy $-\text{O}-$ (used as a connective; cf. epoxy and oxo)
 palmitoyl $\text{CH}_3(\text{CH}_2)_{14}\text{CO}-$ (from *palmitic acid*)
 pentamethylene $-\text{CH}_2(\text{CH}_2)_3\text{CH}_2-$

pentazoyl $\text{N}=\text{N}-\text{N}=\text{N}-\text{N}-$
 pentenyl (like *butenyl*) C_5H_9-
 pentyl = amyl

perseleno $\text{Se}:\text{Se}=\equiv$
 perthio (replacing *O* only) $\text{S}=\text{S}=\equiv$
 phenacyl $\text{C}_6\text{H}_5\text{COCH}_2-$
 phenacylidene $\text{C}_6\text{H}_5\text{COCH}=\equiv$
 phenanthryl C_{14}H_9- (from *phenanthrene*, 6 isomers)
 phenanthrylene $-\text{C}_{14}\text{H}_8-$ (several isomers)
 phenenyl $\text{C}_6\text{H}_3\equiv$ (*s*-, *as*-, *v*-)
 phenethyl $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2-$
 phenetidino $\text{C}_2\text{H}_5\text{OC}_6\text{H}_4\text{NH}-$
 phenetyl (*o*-, *m*-, or *p*-) $\text{C}_2\text{H}_5\text{OC}_6\text{H}_4-$
 phenoxy $\text{C}_6\text{H}_5\text{O}-$
 phenyl C_6H_5-
 phenylazo $\text{C}_6\text{H}_5\text{N}:\text{N}-$
 phenylcarbamido = phenylureido
 phenylene $\text{C}_6\text{H}_4 =$ (*o*-, *m*-, or *p*-)
 phenylenedisazo $-\text{N}:\text{NC}_6\text{H}_4\text{N}:\text{N}-$ (*o*-, *m*-, *p*-)
 phenylidene = cyclohexadienylidene
 phenylureido $\text{C}_6\text{H}_5\text{NHCONH}-$
 phospharseno $-\text{P}:\text{As}-$
 phosphazo $-\text{P}:\text{N}-$
 phosphinico $\text{HOOP}=(\text{from phosphinic acid})$
 phosphino $\text{H}_2\text{P}-$
 phospho $\text{O}_2\text{P}-$
 phosphono $(\text{HO})_2\text{OP}-$
 phosphoro $-\text{P}:\text{P}-$
 phosphoroso $\text{OP}-$
 phthalal = phthalylidene

phthalidene $\text{C}_6\text{H}_4 \cdot \text{CO} \cdot \text{O} \cdot \text{C}=(\text{from phthalide})$

phthalidyl $\text{C}_6\text{H}_4 \cdot \text{CO} \cdot \text{O} \cdot \text{CH}-(\text{from phthalide})$
 phthalimido $\text{C}_6\text{H}_4(\text{CO})_2\text{N}-(\text{o})$
 phthaloyl $-\text{OCC}_6\text{H}_4\text{CO}-(\text{o})$
 phthalylidene $=\text{HCC}_6\text{H}_4\text{CH}=(\text{o})$
 picryl $2,4,6-(\text{NO}_2)_3\text{C}_6\text{H}_2-$
 piperidyl $\text{C}_5\text{H}_{10}\text{N}-(\text{from piperidine}, 4 \text{ isomers})$
 piperonyl $3,4-(\text{CH}_2\text{O})_2\text{C}_6\text{H}_3\text{CH}_2-$
 piperonylidene $3,4-(\text{CH}_2\text{O})_2\text{C}_6\text{H}_3\text{CH}=\equiv$
 pivalyl $(\text{CH}_3)_3\text{CCO}-(\text{from pivalic acid})$
 prolyl (from *proline*)

$\text{NH} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH} \cdot \text{CO}-$
 propargyl = 2-propynyl
 propenyl $\text{CH}_3\text{CH}:\text{CH}-$
 propenylidene $\text{CH}_3\text{CH}:\text{C}=\equiv$
 propiolyl $\text{HC}:\text{CCO}-$
 propionyl $\text{CH}_3\text{CH}_2\text{CO}-$
 propoxy $\text{CH}_3\text{CH}_2\text{CH}_2\text{O}-$
 propyl $\text{CH}_3\text{CH}_2\text{CH}_2-$
 propylene $-\text{CH}(\text{CH}_3)\text{CH}_2-$
 propylidene $\text{CH}_3\text{CH}_2\text{CH}=\equiv$
 1-propynyl $\text{CH}_3\text{C}:\text{C}-$
 2-propynyl $\text{CH}:\text{CCH}_2-$
 pseudoallyl = isopropenyl
as-pseudocumyl $2,3,5-(\text{CH}_3)_3\text{C}_6\text{H}_2-$
s-pseudocumyl $(2,4,5-)$
v-pseudocumyl $(2,3,6-)$
 pseudoindolyl $\text{C}_8\text{H}_6\text{N}-(\text{from pseudoindole}, 7 \text{ isomers})$
 pyranyl $\text{C}_5\text{H}_5\text{O}-(2-\alpha, 2-\gamma, 3-\alpha, \text{etc.})$

pyrazolyl $\text{C}_3\text{H}_3\text{N}_2-(\text{from pyrazole}, 4 \text{ isomers})$
 pyridyl $\text{C}_5\text{H}_4\text{N}-(\text{from pyridine}, 3 \text{ isomers})$
 pyridylidene



4(1)-, etc.

pyrimidyl $\text{C}_4\text{H}_3\text{N}_2-(\text{from pyrimidine})$
 pyromucyl = 2-furoyl
 pyrrolidyl $\text{C}_4\text{H}_5\text{N}-(\text{from pyrrolidine}, 3 \text{ isomers})$

pyrrolyl $\text{CH}:\text{CH}:\text{CH}:\text{CH}:\text{N} \cdot \text{CO}-$
 pyrrol $\text{C}_4\text{H}_4\text{N}-(\text{from pyrrole}, 3 \text{ isomers})$
 quinolyl $\text{C}_9\text{H}_6\text{N}-(\text{from quinoline}, 7 \text{ isomers})$
 quinolyl $\text{C}_6\text{H}_3\text{O}_2-(\text{from quinone})$
 quinoxalyl $\text{C}_8\text{H}_5\text{N}_2-(\text{from quinoxaline})$
 salicyl = *o*-hydroxyphenyl; = *o*-hydroxybenzyl
 salicylidene $\text{HOC}_6\text{H}_4\text{CH}=(\text{o})$
 salicyloyl $\text{HOC}_6\text{H}_4\text{CO}-(\text{o})$
 selenino $(\text{HO})\text{OSe}-$
 seleninyl $\text{OSe}=\equiv$
 seleno $\text{Se}=\equiv$
 selenocyno $\text{NCSe}-$
 selenono $\text{HO}_2\text{Se}-$
 selenoyl $-\text{SeO}_2-$
 selenyl $\text{HSe}-$
 semicarbazido $\text{NH}_2\text{CONHNH}-$
 silico $(\text{HO})\text{OSi}-$
 silicoyl $\text{H}_3\text{Si}-$
 silicylene $\text{H}_2\text{Si}=\equiv$
 stannyl $\text{H}_3\text{Sn}-$
 stearoyl $\text{CH}_3(\text{CH}_2)_{16}\text{CO}-$
 stibarseno $-\text{Sb}:\text{As}-$
 stibinic $\text{HOOSb}=\equiv$
 stibino $\text{H}_2\text{Sb}-$
 stibo $\text{O}_2\text{Sb}-$
 stibono $(\text{HO})_2\text{OSb}-$
 stiboso $\text{O}:\text{Sb}-$
 stibyl = stibino
 stibylene $\text{HSb}=\equiv$
 styrene $-\text{CH}(\text{C}_6\text{H}_5)\text{CH}_2-$
 styrolene = styrene
 styryl $\text{C}_6\text{H}_5\text{CH}:\text{CH}-$
 succinamyl $\text{H}_2\text{NCOCH}_2\text{CH}_2\text{CO}-$
 succinimido $(\text{CH}_2\text{CO})_2\text{N}-$
 succinyl $-\text{OCC}_2\text{H}_4\text{CH}_2\text{CO}-$
 sulfamino $\text{HO}_2\text{SNH}-$
 sulfamyl $\text{H}_2\text{NO}_2\text{S}-$
 sulphydryl = mercapto
 sulfino $\text{HO}_2\text{S}-$
 sulfinyl $\text{OS}=\equiv$
 sulfo $\text{HO}_2\text{S}-$
 sulfonamido $-\text{SO}_2\text{NH}-$
 sulfonyl $-\text{SO}_2-$
 sulfuryl = sulfonyl
 tauryl $\text{H}_2\text{NCH}_2\text{CH}_2\text{SO}_2-$
 telluro $\text{Te}=\equiv$
 terephthalal = terephthalylidene
 terephthaloyl $-\text{OCC}_6\text{H}_4\text{CO}-(\text{p})$
 terephthalylidene $=\text{HCC}_6\text{H}_4\text{CH}=(\text{p})$
 tetramethylene $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$
 tetrazolyl $\text{CHN}_4-(\text{from tetrazole}, 2 \text{ isomers})$
 thenoyl $\text{C}_4\text{H}_3\text{SCO}-(\text{from thiophenecarboxylic acid}, 2 \text{ isomers})$
 thenyl (2 isomers) $\text{C}_4\text{H}_3\text{SCH}_2-$
 thenylidene (2 isomers) $\text{C}_4\text{H}_3\text{SCH}=\equiv$
 thiazolyl $\text{C}_3\text{H}_2\text{NS}-(\text{from thiazole}, 3 \text{ isomers})$
 thienyl $\text{C}_4\text{H}_3\text{S}-(\text{from thiophene}, 2 \text{ isomers})$
 thio $-\text{S}-$
 thiocarbonyl $\text{SC}=\equiv$
 thiocyano $\text{NCS}-$
 thiohydroxy = mercapto

thiol (*S* replacing *O* in *OH*) } Used in place of
 thiono (*S* replacing *O* in *CO*) } "thio" when re-
 quired for distinction

thionyl = sulfinyl
 thuyl $\text{C}_{10}\text{H}_{17}-(\text{from sabinane}, \text{attached at } 2\text{-position})$

thymyl (from thymol)

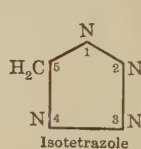
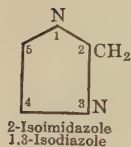
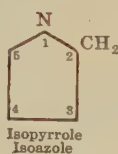
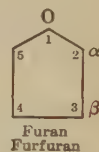
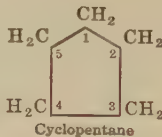
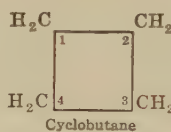
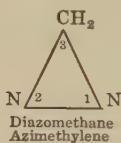
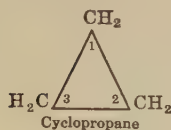
$\text{HC}:\text{C}(\text{CH}_3):\text{CH}:\text{CH}:\text{C}(\text{CH}(\text{CH}_3)_2):\text{C}-$
 toloxy (*o*, *m* or *p*) $\text{CH}_3\text{C}_6\text{H}_4\text{O}-$
 toluino (*o*, *m* or *p*) $\text{CH}_3\text{C}_6\text{H}_4\text{NH}-$
 toluyyl (*o*, *m* or *p*) $\text{CH}_3\text{C}_6\text{H}_4\text{CO}-$
 α -toluyyl $\text{C}_6\text{H}_5\text{CH}_2\text{CO}-$
 tolyl (*o*, *m* or *p*) $\text{CH}_3\text{C}_6\text{H}_4-$
 α -tolyl = benzyl
 tolylene (β isomers) $\text{CH}_3\text{C}_6\text{H}_3=-$
 α -tolylene = benzylidene
 triazeno $\text{NH}_2\text{N}:\text{N}-$
 triazinyl $\text{C}_6\text{H}_2\text{N}_3-$ (from triazine)
 triazo N_3-
 triazolyl $\text{C}_2\text{H}_2\text{N}_3-$ (from triazole)
 trimethylene $-\text{CH}_2\text{CH}_2\text{CH}_2-$
 tryptophyl $\text{C}_{11}\text{H}_{11}\text{N}_2\text{O}-$ (from tryptophan)
 tyrosyl $p\text{-HO}\text{C}_6\text{H}_4\text{CH}_2\text{CHNH}_2\text{CO}-$ (from tyrosine)
 undecyl = hendecyl (in sense $\text{C}_{11}\text{H}_{23}-$)
 uramino = ureido

ureido $\text{H}_2\text{NCONH}-$ (by some used synonymously with ureylene)

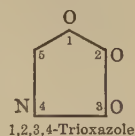
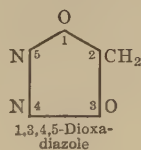
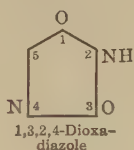
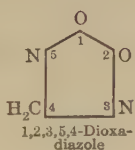
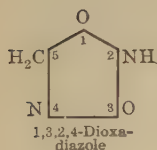
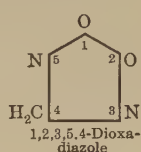
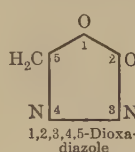
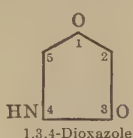
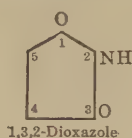
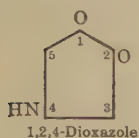
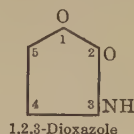
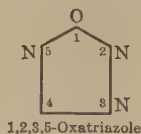
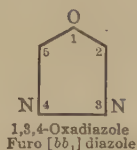
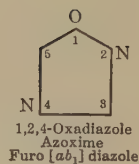
ureylene $-\text{HNCONH}-$
 valeryl $\text{CH}_3(\text{CH}_2)_3\text{CO}-$
 valyl $(\text{CH}_3)_2\text{CHC}(\text{H})(\text{NH}_2)\text{CO}-$ (from valine)
 vanillal = vanillylidene
 vanilloyl 3,4- $(\text{CH}_3\text{O})(\text{HO})\text{C}_6\text{H}_3\text{CO}-$
 vanillyl 3,4- $(\text{CH}_3\text{O})(\text{HO})\text{C}_6\text{H}_3\text{CH}_2-$
 vanillylidene 3,4- $(\text{CH}_3\text{O})(\text{HO})\text{C}_6\text{H}_3\text{CH}=-$
 veratral = veratrylidene
 veratroyl 3,4- $(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CO}-$
 veratryl 3,4- $(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CH}_2-$
 veratrylidene 3,4- $(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CH}=-$
 vinyl $\text{H}_2\text{C}:\text{CH}-$
 vinylene $-\text{CH}:\text{CH}-$
 vinylidene $\text{H}_2\text{C}:\text{C}=-$
 xanthyl $\text{C}_{13}\text{H}_9\text{O}-$ (from xanthene, β isomers)
 xylyl $(\text{CH}_3)_2\text{C}_6\text{H}_3\text{CO}-$ (from xylic acid, 7 isomers)
 xyllyl $(\text{CH}_3)_2\text{C}_6\text{H}_3-$
 xylylene $-\text{H}_2\text{C}\text{C}_6\text{H}_4\text{CH}_2-$

ORGANIC RING SYSTEMS¹

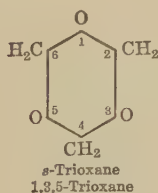
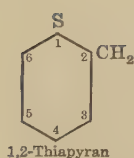
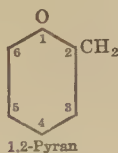
When numbering positions in the case of substitution derivatives of benzoic acid, aniline, phenol, toluene, etc., the characteristic radical of each of these substances (i.e., CO_2H , NH_2 , OH , CH_3 , etc., respectively) is regarded as in position 1.



¹Reprinted by permission from Lange's *Handbook of Chemistry*, Handbook Publishers, Inc., Sandusky, Ohio, 1944.



Sulfur replacing oxygen in these five-membered rings forms the corresponding thiazoles; thiatriazoles; dithiazoles; dithiadiazoles; and trithiazoles.

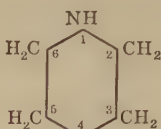




Pyrimidine
1,3-Diazine
Metadiazine
Miazine



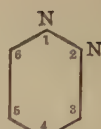
Pyrazine
1,4-Diazine
Paradiazine
Piazine



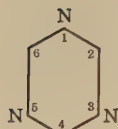
Piperazine
Hexahydro-
1,4-diazine



s-Triazine
1,2,3-Triazine



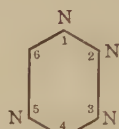
as-Triazine
1,2,4-Triazine



s-Triazine
1,3,5-Triazine
Cyanidine



v-Tetrazine
1,2,3,4-Tetrazine



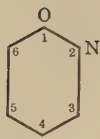
as-Tetrazine
1,2,3,5-Tetrazine



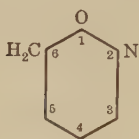
s-Tetrazine
1,2,4,5-Tetrazine



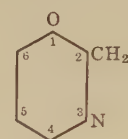
Pentazine



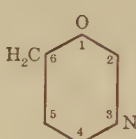
CH₂
1,2,4-Oxazine



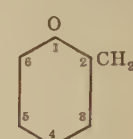
1,2,6-Oxazine



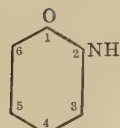
1,3,2-Oxazine



1,3,6-Oxazine
Pentoxazole



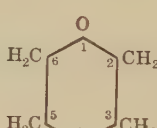
1,4-Oxazine



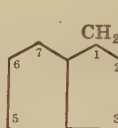
o-Isoxazine



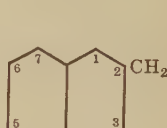
p-Isioxazine



Morpholine
Tetrahydro-
p-isoxazine

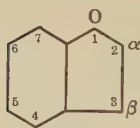


Indene

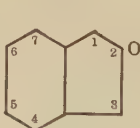


Isoindene

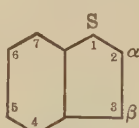
In a similar manner are derived: oxadiazine; oxatriazine; oxatetrazine; dioxazine; dioxadiazine; dioxatriazine; trioxazine; trioxadiazine; tetroxazine. Sulfur replacing oxygen in these rings forms the corresponding thia derivatives.



Benzofuran
Coumarone



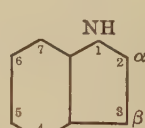
Isobenzofuran



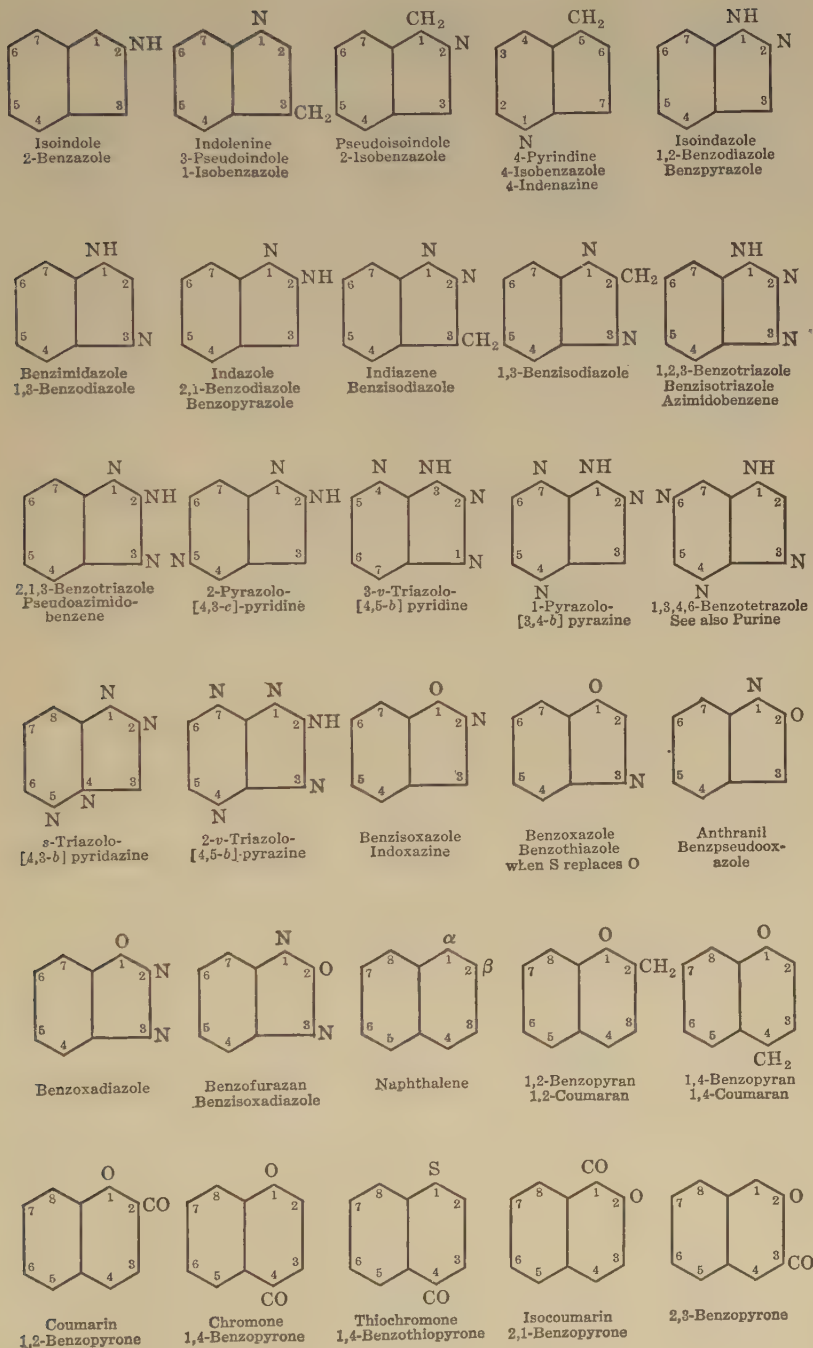
Thionaphthene
Benzothiofuran
Benzothiophene

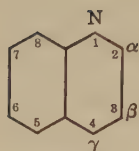


Isothionaphthene
Isobenzothiophene



Indole
1-Benzazole
Benzopyrrole

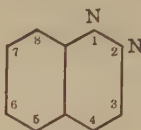




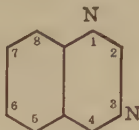
Quinoline
1-Benzazine



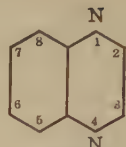
Isoquinoline
2-Benzazine
Leucoline



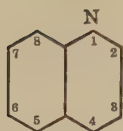
Cinnoline
1,2-Benzodiazine
 α -Phenodiazine



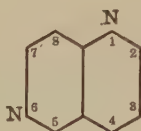
Quinazoline
1,3-Benzodiazine
Pheniazine



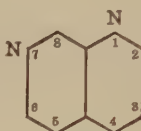
Quinoxaline
1,4-Benzodiazine
Phenplazine



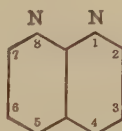
Pyrido[3,2-*b*]-
pyridine



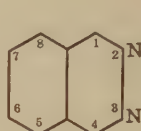
Pyrido[4,3-*b*]-
pyridine



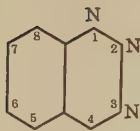
Pyrido[3,4-*b*]-
pyridine



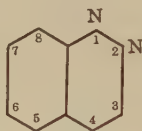
Naphthyridine



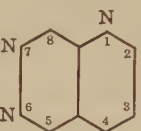
Phthalazine
2,3-Benzodiazine
 β -Phenodiazine



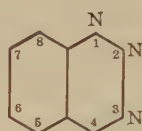
1,2,3-Benzotriazine
Phenotriazine



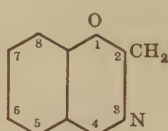
1,2,4-Benzotriazine



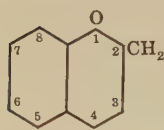
Pyrido[2,3-*d*]-
pyridazine



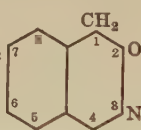
1,2,3,4-Benzotetrazine



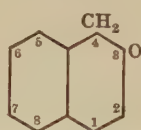
1,3,2-Benzoxazine



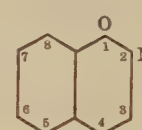
1,4,2-Benzoxazine



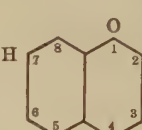
2,3,1-Benzoxazine



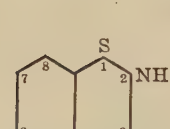
3,1,4-Benzoxazine



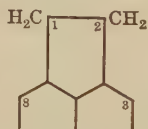
1,2-Benzisoxazine



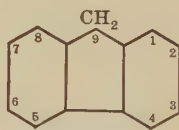
1,4-Benzisoxazine



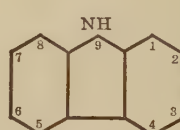
1,2-Benzisothiazine
Also a 1,4-Form



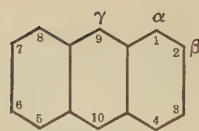
Acenaphthene



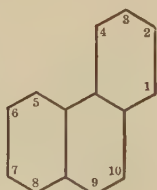
Fluorene
Diphenylenemethane



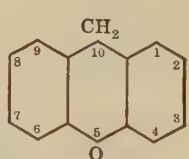
Carbazole
Dibenzopyrrole
Diphenyleneimide



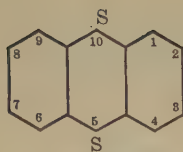
Anthracene



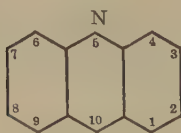
Phenanthrene



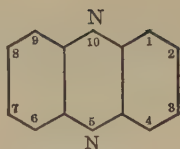
Xanthene



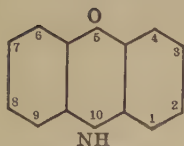
Thianthrene



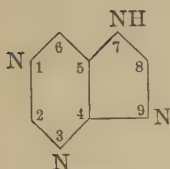
Acridine



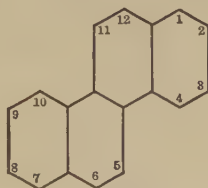
Phenazine

Phenoxazine
S replacing O = Pheno-
thiazine

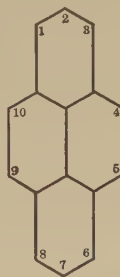
Naphthalene

Spiropentane
Rings with but one
atom in common are known
as "spiro compounds."

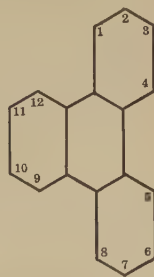
Purine



Chrysene



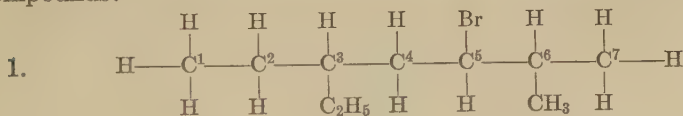
Pyrene



Triphenylene

For a more complete listing of ring systems see Richter's *Lexikon der Kohlenstoffverbindungen*, Vol. I, p. 14 (1910).

We shall now illustrate some of the methods employed in naming compounds:



(a) In naming this compound, first select the longest straight chain. In this case, it would be a seven-carbon chain. Therefore, the naming will center around the saturated hydrocarbon heptane.

(b) Consider the elements and groups other than hydrogen as substituents.

(c) Therefore the name of this compound becomes:

3-ethyl-6-methyl-5-bromoheptane



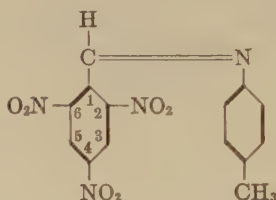
(a) Selecting the longest chain, we have four carbon atoms.


(b) Since there are two double bonds in this chain, the name of the compound must end in *-diene* and center around the unsaturated hydrocarbon butadiene.

(c) The name of this compound becomes 2-methylbutadiene.

(d) But to indicate the positions of the double bonds, the final name becomes 2-methyl-1,3-butadiene (isoprene).

3.



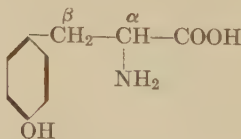
(a) This compound contains the benzal  (divalent) group where-

in the three hydrogens in positions 2, 4, 6 are replaced by three nitro groups.

(b) In addition, we have *p*-toluidine, where, in place of the two hydrogens in the amino group, there is a double bond.

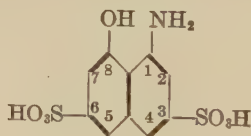
(c) Therefore, the name of this compound becomes 2,4,6-trinitrobenzal-*p*-toluidine.

4.



This compound is named α -amino- β -*p*-hydroxyphenylpropionic acid (tyrosine), because it has an amino group attached to the α -carbon atom and the *p*-hydroxyphenyl group attached to the β -carbon atom.

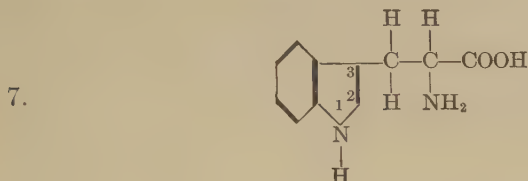
5.



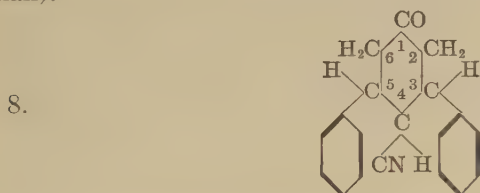
This compound is named 1-amino-8-hydroxy-3,6-naphthalenedisulfonic acid ("H-acid").



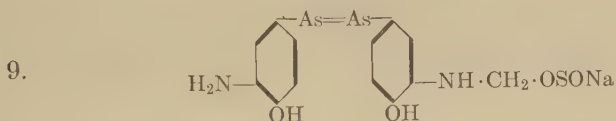
This compound is named 1,4-dihydroxyanthraquinone (quinizarin).



This compound is named α -amino- β -3-indolepropionic acid (tryptophan).



This compound is named 3,5-diphenyl-4-cyanocyclohexanone-1.



This compound is named sodium 3,3'-diamino-4,4'-dihydroxyarsenobenzene-N-methylenesulfinate.

APPENDIX

GLOSSARY

Active principles include such natural products as carbohydrates, alkaloids, glucosides, organic acids, resins, oils and fats, volatile oils, protein bodies, and ferments.

Analgesics are drugs that, when absorbed into the blood, relieve pain.

Anesthetics are drugs that produce insensibility to pain. (Local anesthetics are drugs that produce insensibility to pain at the site of application.)

Anodynes are drugs that relieve pain when applied locally. They are usually milder in action than the analgesics.

Antacids are drugs that neutralize acids.

Antidote is an agent that affects a poison, either physically or chemically or both, so as to remove it from the body or alter its character by forming with it an insoluble or inert compound.

Antifebrin is another name for acetanilide (used to decrease fever).

Antipyretics are drugs that reduce fever.

Antiscorbutic is an agent effective against scurvy.

Antiseptics are substances that check the growth of bacteria.

Antispasmodics are drugs that lessen contractions of muscles and also lessen convulsions.

Aperients are substances that produce mild movements of the bowels.

Aromatics are spicy substances that increase the secretion of the stomach and the intestines.

Astringents are drugs that contract or harden the tissues.

Bactericide is an agent that destroys bacteria.

Bacteriostatic substance is one that prevents the growth of bacteria.

Balsams are semi-fluid, resinous, and fragrant vegetable juices of many varieties.

Bitters are drugs that increase the appetite because of their bitter taste.

Carcinogenic substance is one producing cancer in living tissues.

Cardiac depressants are drugs that lessen the heart action.

Cardiac stimulants are drugs that increase the activity of the heart.

Carminatives are drugs that produce a feeling of comfort in the stomach and relieve the formation of gas in the stomach and the intestines.

Catabolism is the breaking down of tissue material in the body.

Cathartics are drugs that cause movements of the bowels.

Caustics are substances that burn or destroy tissues.

Counterirritants are drugs that counteract irritation of the skin.

Cyanosis signifies "bluing" of the skin.

Deodorants are remedies that destroy unpleasant odors.

Disinfectants are drugs that check the growth of bacteria.

Diuretics are drugs that increase the flow of urine.

Emetics are drugs that produce vomiting.

- Expectorants** are drugs that increase coughing and bronchial secretions.
- Febrifuges** are drugs that reduce fever.
- Fungicide** is an agent that destroys spores and fungi.
- Gums** are amorphous, transparent substances, which are widely disseminated in plants.
- Hemostatics** are substances that check bleeding.
- Hypnotics** are drugs that induce sleep.
- Lachrymator** is a substance that produces the secretion and discharge of tears.
- Lacteal** is any one of the intestinal lymphatics that absorbs fats.
- Laxatives** are drugs that produce mild movements of the bowels.
- Mydriatics** are drugs that widen (dilate) the pupil of the eye.
- Myotics** are drugs that narrow (contract) the pupil of the eye.
- Narcosis** is the state of profound unconsciousness produced by a drug.
- Narcotic** is a drug that produces stupor or complete insensibility.
- Parasiticide** is an agent that destroys the animal and vegetable parasites found upon the human body.
- Peristalsis** is the wormlike movement by which the alimentary canal propels its contents.
- Plasticizer** is any compound that keeps a material soft and viscous.
- Plastics** are synthetic materials that are shaped when soft and that harden on cooling.
- Purgatives** are drugs that produce moderately active and frequent movements of the bowels.
- Putrefaction** is the decomposition of animal or vegetable substances effected largely through microorganisms, and resulting in the production of various solids, liquids, and gases, some of which have a foul odor.
- Pyrolysis** is the decomposition of organic substances by heat.
- Refrigerants** are substances that relieve thirst and reduce fever.
- Resins** are complex organic resinous substances.
- Respiratory depressants** are drugs that lessen the frequency and depth of breathing.
- Respiratory stimulants** are drugs that increase the depth and frequency of breathing.
- Rubefaciants** are drugs that redden the skin by widening (dilating) the capillaries.
- Sedatives** are drugs that lessen the activity of an organ or part of the body.
- Somnifaciants** or **soporifics** are drugs that induce sleep.
- Styptics** are substances that stop bleeding.
- Trypanocides** destroy certain parasites found in the blood of man and of animals.
- Vaso-constrictor** is a drug that increases arterial pressure.
- Vaso-dilator** is a drug that lowers arterial pressure.
- Vermicides** are drugs that destroy worms.
- Vermifuge** is a drug that expels worms or intestinal parasites.
- Vertigo** means dizziness.
- Vesicatories** or **vesicants** are substances that produce blisters.
- Wetting agents** increase or speed up the penetrating power of liquids, and facilitate wetting or adhesion of a liquid on a solid, usually by decreasing the surface tension.

INTERNATIONAL ATOMIC WEIGHTS

1943

Reprinted from the *Journal of the American Chemical Society*

	Sym- bol	Atomic Number	Atomic Weight		Sym- bol	Atomic Number	Atomic Weight
Aluminum...	Al	13	26.97	Molybdenum..	Mo	42	95.95
Antimony....	Sb	51	121.76	Neodymium..	Nd	60	144.27
Argon.....	A	18	39.944	Neon.....	Ne	10	20.183
Arsenic.....	As	33	74.91	Nickel.....	Ni	28	58.69
Barium.....	Ba	56	137.36	Nitrogen.....	N	7	14.008
Beryllium....	Be	4	9.02	Osmium.....	Os	76	190.2
Bismuth.....	Bi	83	209.00	Oxygen.....	O	8	16.0000
Boron.....	B	5	10.82	Palladium....	Pd	46	106.7
Bromine.....	Br	35	79.916	Phosphorus... P	15	30.98	
Cadmium....	Cd	48	112.41	Platinum.....	Pt	78	195.23
Calcium.....	Ca	20	40.08	Potassium....	K	19	39.096
Carbon.....	C	6	12.010	Praseodymium	Pr	59	140.92
Cerium.....	Ce	58	140.13	Protactinium..	Pa	91	231
Cesium.....	Cs	55	132.91	Radium.....	Ra	88	226.05
Chlorine....	Cl	17	35.457	Radon.....	Rn	86	222
Chromium... Cr	24	52.01	Rhenium.....	Re	75	186.31	
Cobalt.....	Co	27	58.94	Rhodium.....	Rh	45	102.91
Columbium.. Cb	41	92.91	Rubidium....	Rb	37	85.48	
Copper.....	Cu	29	63.57	Ruthenium... Ru	44	101.7	
Dysprosium.. Dy	66	162.46	Samarium....	Sm	62	150.43	
Erbium.....	Er	68	167.2	Scandium....	Sc	21	45.10
Europium....	Eu	63	152.0	Selenium.....	Se	34	78.96
Fluorine....	F	9	19.00	Silicon.....	Si	14	28.06
Gadolinium.. Gd	64	156.9	Silver.....	Ag	47	107.880	
Gallium.....	Ga	31	69.72	Sodium.....	Na	11	22.997
Germanium.. Ge	32	72.60	Strontium....	Sr	38	87.63	
Gold.....	Au	79	197.2	Sulfur.....	S	16	32.06
Hafnium.....	Hf	72	178.6	Tantalum....	Ta	73	180.88
Helium.....	He	2	4.003	Tellurium....	Te	52	127.61
Holmium....	Ho	67	164.94	Terbium.....	Tb	65	159.2
Hydrogen....	H	1	1.0080	Thallium....	Tl	81	204.39
Indium.....	In	49	114.76	Thorium.....	Th	90	232.12
Iodine.....	I	53	126.92	Thulium.....	Tm	69	169.4
Iridium.....	Ir	77	193.1	Tin.....	Sn	50	118.70
Iron.....	Fe	26	55.85	Titanium....	Ti	22	47.90
Krypton.....	Kr	36	83.7	Tungsten....	W	74	183.92
Lanthanum.. La	57	138.92	Uranium.....	U	92	238.07	
Lead.....	Pb	82	207.21	Vanadium....	V	23	50.95
Lithium.....	Li	3	6.940	Xenon.....	Xe	54	131.3
Lutecium....	Lu	71	174.99	Ytterbium....	Yb	70	173.04
Magnesium.. Mg	12	24.32	Yttrium.....	Y	39	88.92	
Manganese... Mn	25	54.93	Zinc.....	Zn	30	65.38	
Mercury.....	Hg	80	200.61	Zirconium....	Zr	40	91.22

BOILING AND MELTING POINTS OF A NUMBER OF ORGANIC COMPOUNDS

Since very few physical constants are given in the body of the work, we shall give here the boiling and melting points of a number of compounds which the student is likely to encounter.¹

Name	m.p., °C	b.p., °C
Acetaldehyde	-120	21
Acetamide	82	222
Acetanilide	114	305
Acetic acid	16.7	119
Acetic anhydride	-73	139
Acetone	-94	55.6
Acetonitrile	-45	81
Acetyl chloride	-112	55
Allyl alcohol	-129	96
Amyl acetate	-75	148
Aniline	-6.5	184.4
Aniline hydrochloride	198	245
Anthracene	216	360
Anthraquinone	285	380
Benzaldehyde	-13.5	179
Benzene	5.4	80.4
Benzenesulfonic acid	52	Decomposes
Benzidine	127	400
Benzoic acid	121	249
Butyl alcohol	-79	116
Camphor	176	209
Carbon disulfide	-111	46
Carbon tetrachloride	-23	78
Chloroform	-63	61
Cinnamic acid	133	300
Citric acid	153	Decomposes
<i>o</i> -Cresol	30	191
<i>m</i> -Cresol	11	202
<i>p</i> -Cresol	35	202
<i>p</i> -Cymene	-73	175
Dimethylaniline	2	194
Diphenyl	70.5	254
Ethyl acetate	-82	77
Ethyl alcohol	-114	78.4
Ethyl bromide	-115	38
Ethyl butyrate	-93	120

¹ For others, consult handbooks of chemistry (p. 431).

Name	m.p., °C	b.p., °C
Ethyl chloride	-140	12.5
Ethyl ether	-116	35
Ethyl iodide	-118	72
Ethylene glycol	-17	199
Formaldehyde	-21
Formic acid	7.5	100
Furfural	-36	55 (17 mm)
Glucose	146	Decomposes
Glycerol	17	291
Hydrocyanic acid	-10	26
Iodoform	119	Sublimes
Isoamyl alcohol	-117	131
Isopropyl alcohol	-85	83
Lactic acid	18	119 (12 mm)
Methanol	-95	65
Methyl iodide	-66	45
Methyl salicylate	-8	222
Naphthalene	80	218
α -Naphthol	96	279
β -Naphthol	122	285
α -Naphthylamine	50	300
β -Naphthylamine	111	306
Nitrobenzene	5	210.8
Oxalic acid	189	150 Sublimes
Phenol	45	182.6
Phthalic acid	213	
Phthalic anhydride	131	284.5
Pyridine	-42	116
Pyrogallol	132.5	293
Resorcinol	118	280
Saccharin	228	Sublimes
	Decomposes	
Salicylic acid	157	Sublimes
Sulfanilic acid	288	Decomposes
Thymol	50	231.8
Toluene	-93	111
<i>o</i> -Toluidine	-21	199.7
<i>m</i> -Toluidine	-13	203
<i>p</i> -Toluidine	45	200
Urea	132	Decomposes
Vanillin	81	285
		Decomposes
<i>o</i> -Xylene	-27	144
<i>m</i> -Xylene	-53	139
<i>p</i> -Xylene	15	138

DISSOCIATION CONSTANTS OF ACIDS *

Acid	Formula	Constant for the First Hydrogen	Temp. °C	Constant for the Second Hydrogen	Temp. °C
Acetic	$C_2H_4O_2$	1.86×10^{-5}	25		
α -Alanine	$C_3H_7O_2N$	9×10^{-10}	25		
Arsenic	H_3AsO_4	5×10^{-8}	25	4×10^{-5} $6 \times 10^{-10}(3H)$	25 25
Arsenious	$HAsO_2$	6×10^{-10}	25		
Barbituric	$C_4H_4O_3N$	1.05×10^{-4}	25		
Benzoic	$C_7H_6O_2$	6.6×10^{-5}	25		
Boric	H_3BO_3	6.4×10^{-10}	25		
Bromoacetic	$C_2H_3O_2Br$	1.38×10^{-3}	25		
α -Bromopropionic	$C_3H_5O_2Br$	1.08×10^{-3}	25		
β -Bromopropionic	$C_3H_5O_2Br$	9.8×10^{-5}	25		
Butyric	$C_4H_8O_2$	1.48×10^{-5}	25		
Carbonic	H_2CO_3	3×10^{-7}	18	6×10^{-11}	25
Chloroacetic	$C_2H_3O_2Cl$	1.55×10^{-3}	25		
α -Chloropropionic	$C_3H_5O_2Cl$	1.47×10^{-3}	25		
β -Chloropropionic	$C_3H_5O_2Cl$	8.59×10^{-5}	25		
Citric	$C_6H_8O_7$	8×10^{-4}	25		
Dichloroacetic	$C_2H_2O_2Cl_2$	5×10^{-2}	25		
Formic	CH_2O_2	2.14×10^{-4}	25		
Fumaric	$C_4H_4O_4$	1×10^{-3}	25	3×10^{-5}	25
Hippuric	$C_9H_9O_3N$	2.3×10^{-4}	25		
Hydrocyanic	CHN	7.2×10^{-10}	25		
Hydroquinone	$C_6H_6O_2$	1.1×10^{-10}	18		
Hydrosulfuric	H_2S	9.1×10^{-8}	18	1.2×10^{-15}	
Hypochlorous	$HOCl$	3.7×10^{-8}	17		
Iodic	HIO_3	1.9×10^{-1}	25		
Isobutyric	$C_4H_8O_2$	1.5×10^{-5}	25		
Isovaleric	$C_5H_{10}O_2$	1.7×10^{-5}	25		
Lactic	$C_3H_6O_3$	1.38×10^{-4}	25		
Maleic	$C_4H_4O_4$	1.5×10^{-2}	25	2.6×10^{-7}	25
Malic	$C_4H_6O_5$	4×10^{-4}	25	9×10^{-6}	25
Malonic	$C_3H_4O_4$	1.61×10^{-3}	25	2.1×10^{-6}	25
Mandelic	$C_8H_8O_3$	4.29×10^{-4}	25		
α -Naphthoic	$C_{11}H_8O_2$	2×10^{-4}	25		
β -Naphthoic	$C_{11}H_8O_2$	6.8×10^{-5}	25		
Nicotinic	$C_6H_5O_2N$	1.4×10^{-5}	25		
Nitrous	HNO_2	4×10^{-4}	18		
Oxalic	$H_2C_2O_4$	3.8×10^{-2}	25	4.9×10^{-5}	25
Periodic	HIO_4	2.3×10^{-2}	25		
Phenol	C_6H_6O	1.3×10^{-10}	25		
Phosphoric	H_3PO_4	1.1×10^{-2}	18	2×10^{-7} $3.6 \times 10^{-13}(3H)$	18 18
Phosphorous	H_3PO_3	5×10^{-2}	25	2×10^{-5}	25
Phthalic	$C_8H_6O_4$	1.26×10^{-3}	25	3.1×10^{-6}	25
Picolinic	$C_6H_5O_2N$	3×10^{-6}	25		
Picric	$C_6H_3O_7N_3$	1.6×10^{-1}	18		
Propionic	$C_3H_6O_2$	1.4×10^{-5}	25		
Pyromucic (furoic)	$C_5H_4O_3$	7.1×10^{-4}	25		
Pyrophosphoric	$H_4P_2O_7$	1.4×10^{-1}	18	1.1×10^{-2} $2.9 \times 10^{-7}(3H)$ $3.6 \times 10^{-9}(4H)$	18 18 18
Pyrotartaric	$C_6H_8O_4$	8.7×10^{-5}	25		
Salicylic	$C_7H_6O_3$	1.06×10^{-3}	25	1×10^{-13}	20
Selenious	H_2SeO_3	3×10^{-3}	25	5×10^{-8}	25
Succinic	$C_4H_6O_4$	6.6×10^{-5}	25	2.8×10^{-6}	25
Sulfanilic	$C_6H_7O_3NS$	6.2×10^{-4}	25		
Sulfuric	H_2SO_4	2×10^{-2}	18
Sulfurous	H_2SO_3	1.7×10^{-2}	25	5×10^{-6}	25
Tartaric	$C_4H_6O_6$	1.1×10^{-3}	25	6.9×10^{-5}	25
Telluric	H_2TeO_6	6×10^{-7}	25	4×10^{-11}	25
Tellurous	H_2TeO_3	3×10^{-3}	25	2×10^{-8}	25
Trichloroacetic	$C_2HCl_3O_2$	2×10^{-1}	18		
Uric	$C_5H_4O_3N_4$	1.5×10^{-6}	25		
Valeric	$C_5H_{10}O_2$	1.6×10^{-5}	25		

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DISSOCIATION CONSTANTS OF BASES *

Name	Formula	Constant for First OH	Temp. °C	Constant for Second OH	Temp. °C
Acetamide	C_2H_5ON	3.1×10^{-15}	25		
Acetanilide	C_8H_9ON	4.1×10^{-14}	40		
α -Alanine	$C_3H_7O_2N$	5.1×10^{-12}	25		
<i>o</i> -Aminobenzoic	$C_7H_7O_2N$	1.4×10^{-12}	25		
Ammonium hydroxide	NH_4OH	1.8×10^{-5}	25		
Aniline	C_6H_7N	4.6×10^{-10}	25		
Arsenious oxide	As_2O_3	1×10^{-14}	25		
Beryllium hydroxide	$Be(OH)_2$	5×10^{-11}	25
Brucine	$C_{23}H_{25}O_4N_2$	7.2×10^{-4}	25	2.5×10^{-11}	25
Butylamine (sec.)	$C_4H_{11}N$	4.4×10^{-4}	25		
Caffeine	$C_8H_{10}O_2N_4$	4.1×10^{-14}	40		
Cinchonine	$C_{19}H_{22}ON_2$	1.6×10^{-7}	15	3.3×10^{-10}	15
Cocaine	$C_{17}H_{21}O_4N$	4×10^{-7}	25		
Diethylbenzylamine	$C_{11}H_{17}N$	3.6×10^{-5}	25		
Diethylamine	$C_4H_{11}N$	1.26×10^{-3}	25		
Diisoamylamine	$C_{10}H_{23}N$	9.6×10^{-4}	25		
Diisobutylamine	$C_8H_{19}N$	4.8×10^{-4}	25		
Dimethylamine	C_2H_7N	7.4×10^{-4}	25		
Dimethylbenzylamine	$C_9H_{13}N$	1.05×10^{-5}	25		
Dipropylamine	$C_6H_{15}N$	1.02×10^{-3}	25		
Ethylamine	C_2H_7N	5.6×10^{-4}	25		
Ethylenediamine	$C_2H_8N_2$	8.5×10^{-5}	25		
Hydrazine	$N_2H_4 \cdot H_2O$	3×10^{-6}	25		
Isoamylamine	$C_5H_{13}N$	5×10^{-4}	25		
Isobutylamine	$C_4H_{11}N$	3.1×10^{-4}	25		
Isopropylamine	C_3H_9N	5.3×10^{-4}	25		
Lead hydroxide	$Pb(OH)_2$	3×10^{-8}	25
Methylamine	CH_5N	5×10^{-4}	25		
Methyldiethylamine	$C_6H_{13}N$	2.7×10^{-4}	25		
α -Naphthylamine	$C_{10}H_9N$	9.9×10^{-11}	25		
β -Naphthylamine	$C_{10}H_9N$	2×10^{-10}	25		
<i>o</i> -Phenylenediamine	$C_6H_8N_2$	3.3×10^{-10}	25		
Phenylhydrazine	$C_6H_8N_2$	1.6×10^{-9}	40		
Piperidine	$C_5H_{11}N$	1.6×10^{-3}	25		
Propylamine (norm.)	C_3H_9N	4.7×10^{-4}	25		
Pyridine	C_5H_5N	2.3×10^{-9}	25		
Quinine	$C_{20}H_{24}O_2N_2$	2.2×10^{-7}	15	3.3×10^{-10}	15
Quinoline	C_9H_7N	1×10^{-9}	25		
Semicarbazide	CH_5ON_3	2.7×10^{-11}	40		
Silver hydroxide	$AgOH$	1.1×10^{-4}	25		
Strychnine	$C_{21}H_{22}O_4N_2$	1×10^{-7}	15	6×10^{-11}	15
Tetramethylenediamine	$C_4H_{12}N_2$	5.1×10^{-4}	25		
Thiourea	CH_4N_2S	1.1×10^{-15}	25		
<i>m</i> -Toluidine	C_7H_9N	5.5×10^{-10}	25		
<i>o</i> -Toluidine	C_7H_9N	3.3×10^{-10}	25		
<i>p</i> -Toluidine	C_7H_9N	2×10^{-9}	25		
Triethylamine	$C_6H_{15}N$	6.4×10^{-4}	25		
Triisobutylamine	$C_{12}H_{27}N$	2.6×10^{-4}	25		
Trimethylamine	C_3H_9N	7.4×10^{-5}	25		
Trimethylenediamine	$C_3H_{10}N_2$	3.5×10^{-4}	25		
Tripropylamine	$C_9H_{21}N$	5.5×10^{-4}	25		
Urea	CH_4ON_2	1.5×10^{-14}	25		
Zinc hydroxide	$Zn(OH)_2$	1.5×10^{-9}	25

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REFERENCE BOOKS

GENERAL ORGANIC CHEMISTRY TEXTBOOKS

A few representative elementary textbooks are:

- CALDWELL, *Organic Chemistry*, Houghton Mifflin.
CHAMBERLAIN, *Organic Chemistry*, Blakiston.
CONANT, *Chemistry of Organic Compounds*, Macmillan.
FUSON, CONNOR, PRICE, and SNYDER, *A Brief Course in Organic Chemistry*, Wiley
FUSON and SNYDER, *Organic Chemistry*, Wiley.
HILL and KELLEY, *Organic Chemistry*, Blakiston.
JENKINS and HARTUNG, *Chemistry of Organic Medicinal Products*, Wiley.
LUCAS, *Organic Chemistry*, American Book.
MACY, *Organic Chemistry Simplified*, Chemical Publishing Co.
PERKIN and KIPPING, *Organic Chemistry*, Crowell.
PORTER and STEWART, *Organic Chemistry*, Ginn.
RAY, *Organic Chemistry*, Lippincott.
REID, *College Organic Chemistry*, Van Nostrand.
RICHTER, *Textbook of Organic Chemistry*, Wiley.
TAYLOR, *Reactions and Symbols of Carbon Compounds*, Century.
WERTHEIM, *Textbook of Organic Chemistry*, Blakiston.

Some useful study books are:

- HUNTRESS, *Problems in Organic Chemistry*, McGraw-Hill.
LOWY and DOWNEY, *Study Questions in Elementary Organic Chemistry*, Van Nostrand.
UNDERWOOD, *Problems in Organic Chemistry*, McGraw-Hill.

More advanced textbooks are:

- ADAMS, *Organic Reactions*, Vols. I and II, Wiley.
BAKER, *Tautomerism*, Van Nostrand.
BERNTHSEN, *Textbook of Organic Chemistry*, Van Nostrand.
COHEN, *Organic Chemistry for Advanced Students*, Longmans.
FIESER and FIESER, *Organic Chemistry*, Heath.
FRANKLIN, *Nitrogen System of Compounds*, Reinhold.
GILMAN, *Organic Chemistry*, Wiley.
HICKINBOTTOM, *Reactions of Organic Compounds*, Longmans.
JAEGER, *Spatial Arrangements of Atomic Systems and Optical Activity*, McGraw-Hill.
KARRER, *Organic Chemistry*, Nordeman. (Translation from the German.)
MEYER and JACOBSON, *Lehrbuch der organischen Chemie*, Veit, Leipzig.
PORTER, *Molecular Rearrangements*, Reinhold.
PRINGSHEIM, *The Chemistry of the Saccharides*, McGraw-Hill.
RICHTER, *Organic Chemistry*, Nordeman. (Translation from the German.)

SAUNDERS, *The Aromatic Diazo Compounds*, Longmans.

SCHMIDT and RULE, *A Textbook of Organic Chemistry*, Van Nostrand.

SIDGWICK, TAYLOR, and BAKER, *Organic Chemistry of Nitrogen*, Oxford University Press.

STEWART, *Recent Advances in Organic Chemistry*, Longmans.

WATSON, *Modern Theories of Organic Chemistry*, Oxford University Press.

WHITMORE, *Organic Chemistry*, Van Nostrand.

LABORATORY MANUALS

Several representative laboratory manuals are:

ADAMS and JOHNSON, *Elementary Laboratory Experiments in Organic Chemistry*, Macmillan.

ADKINS and McELVAIN, *Practice of Organic Chemistry*, McGraw-Hill.

COGHILL and STURTEVANT, *An Introduction to the Preparation and Identification of Organic Compounds*, McGraw-Hill.

COHEN, *Practice of Organic Chemistry*, Macmillan.

COLBERT, *Laboratory Technique of Organic Chemistry*, Appleton-Century.

FIESER, *Experiments in Organic Chemistry*, Heath.

FISHER, *Laboratory Manual of Organic Chemistry*, Wiley.

GATTERMANN and WIELAND, *Laboratory Methods of Organic Chemistry*, Macmillan.

LOWY and BALDWIN, *A Laboratory Manual of Elementary Organic Chemistry*, Wiley.

NORRIS, *Experimental Organic Chemistry*, McGraw-Hill.

PORTER and STEWART, *Organic Chemistry for the Laboratory*, Ginn.

ROBERTSON, *Laboratory Practice of Organic Chemistry*, Macmillan.

WERTHEIM, *Laboratory Guide for Organic Chemistry*, Blakiston.

WILLIAMS and BREWSTER, *Laboratory Manual of Organic Chemistry*, Van Nostrand.

More advanced or extended manuals are:

HEIDELBERGER, *Advanced Laboratory Manual of Organic Chemistry*, Reinhold.

HCUBEN and WEYL, *Die Methoden der organischen Chemie*, Thieme, Leipzig.

LASSAR-COHN, *Arbeitsmethoden für organisch-chemische Laboratorien*, Voss, Hamburg.

VANINO, *Handbuch der präparativen Chemie*, Enke, Stuttgart. (Volume II is devoted to organic chemistry.)

Organic Syntheses, Wiley, is an annual publication of carefully tested (and checked) organic preparations. Two collective volumes include all the preparations through 1939, and literature citations through 1942.

ANALYTICAL CHEMISTRY BOOKS

The following books deal with the analysis of pure organic compounds:

CAMPBELL, *Qualitative Organic Chemistry*, Van Nostrand.

CLARKE, *Organic Analysis*, Longmans.

COLEMAN and ARNALL, *Preparation and Analysis of Organic Compounds*, Blakiston.

KAMM, *Qualitative Organic Analysis*, Wiley.

KINGSCOTT and KNIGHT, *Methods of Quantitative Organic Analysis*, Longmans.

MIDDLETON, *Systematic Qualitative Organic Analysis*, Longmans.

SHRINER and FUSON, *The Systematic Identification of Organic Compounds*, Wiley.

THORPE and WHITELEY, *Organic Chemical Analysis*, Longmans.

For micro methods, the following are suggested:

NIEDERL and NIEDERL, *Micromethods of Quantitative Organic Elementary Analysis*, Wiley.

PREGL, *Quantitative Organic Microanalysis*, Blakiston.

A standard reference work is:

MULLIKEN, *Identification of Pure Organic Compounds*, Wiley. (Volume 3 on dye-stuffs is out of print. The first volume has been rewritten by HUNTRESS.)

Books on applied organic analysis include:

ALLEN, *Commercial Organic Analysis*, Blakiston.

ANON., *Methods of Analysis of the Association of Official Agricultural Chemists (A.O.A.C.)*. (Published every five years.)

AUTENRIETH, *Detection of Poisons and Powerful Drugs*, Blakiston.

BROWNE and ZERBAN, *Physical and Chemical Methods of Sugar Analysis*, Wiley.

ENGELDER, *Laboratory Manual of Gas, Oil, and Fuel Analysis*, Wiley.

FULLER, *The Quantitative Analysis of Medicinal Preparations*, Wiley.

GILL, *Oil Analysis*, Lippincott.

GRIFFIN, *Technical Methods of Analysis*, McGraw-Hill.

LEACH and WINTON, *Food Inspection and Analysis*, Wiley.

LEWKOWITSCH, *Chemical Technology and Analysis of Oils, Fats, and Waxes*, Macmillan.

SCOTT, *Standard Methods of Chemical Analysis*, Van Nostrand.

SHERMAN, *Organic Analysis*, Macmillan.

WOODMAN, *Food Analysis*, McGraw-Hill.

CHEMISTRY AND BIOLOGY

Several books dealing with phases of biochemistry are:

BALDWIN, *An Introduction to Comparative Biochemistry*, Cambridge University Press.

BODANSKY, *Introduction to Physiological Chemistry*, Wiley.

CAMERON, *A Textbook of Biochemistry*, Macmillan.

CANTAROW and TRUMPER, *Clinical Biochemistry*, Saunders.

FIESER, *The Chemistry of Natural Products Related to Phenanthrene*, Reinhold.

GORTNER, *Outlines of Biochemistry*, Wiley.

HARROW, *Biochemistry*, Saunders.

HARROW and SHERWIN, *A Textbook of Biochemistry*, Saunders.

HAWK and BERGEIM, *Practical Physiological Chemistry*, Blakiston.

KOCH, *Practical Methods of Biochemistry*, Wood.

MALISOFF, *A Dictionary of Biochemistry*, Philosophical Library.

MATHEWS, *Physiological Chemistry*, Wood.

STUHLMAN, *Introduction to Biophysics*, Wiley.

WILLIAMS, *Introduction to Biochemistry*, Van Nostrand.

Several books more closely related to medicine are:

DORLAND, *Medical Dictionary*, Saunders.

MACLEOD, *Physiology and Biochemistry in Modern Medicine*, Mosby.

TODD and SANFORD, *Clinical Diagnosis by Laboratory Methods*, Saunders.

WELLS, *Chemical Pathology*, Saunders.

Books dealing with the food problem are:

- ANON., *Food and Life*, Yearbook of Agriculture, 1939; published by the U.S. Dept. of Agriculture.
 BAILEY, *Food Products*, Blakiston.
 JACOBS, *Chemical Analysis of Food and Food Products*, Van Nostrand.
 SHERMAN and LANFORD, *Essentials of Nutrition*, Macmillan.

PHYSICAL CHEMISTRY IN RELATION TO ORGANIC CHEMISTRY

In this field, wide in scope, several books may be included:

- BRANCH and CALVIN, *The Theory of Organic Chemistry*, Prentice-Hall.
 CLARK, *Determination of Hydrogen Ions*, Williams & Wilkins.
 FINDLAY, *Physical Chemistry and Its Applications in Medical and Biological Sciences*, Longmans.
 GETMAN and DANIELS, *Outlines of Physical Chemistry*, Wiley.
 HAMMETT, *Physical Organic Chemistry*, McGraw-Hill.
 HITCHCOCK, *Physical Chemistry*, Thomas.
 JOHLIN, *Introduction to Physical Biochemistry*, Hoeber.
 LOEB, *Proteins and the Theory of Colloid Behavior*, McGraw-Hill.
 REMICK, *Electronic Interpretations of Organic Chemistry*, Wiley.
 SPEAKMAN, *Introduction to the Modern Theory of Valency*, Longmans.
 SUGDEN, *The Parachor and Valency*, Knopf.
 WEST, *Physical Chemistry for Students of Biochemistry and Medicine*, Macmillan.
 WHELAND, *The Theory of Resonance*, Wiley.

APPLIED ORGANIC CHEMISTRY

The field here is enormous. Some selections are presented. For general industrial references, see:

- GREGORY, *Uses and Applications of Chemical and Related Materials*, Reinhold.
 GROGGINS, *Unit Processes in Organic Synthesis*, McGraw-Hill.
 READ, *Industrial Chemistry*, Wiley.
 RIEGEL, *Industrial Chemistry*, Wiley.
 ROGERS, *Industrial Chemistry*, Van Nostrand.
 SHREVE, *The Chemical Process Industries*, McGraw-Hill.
 THORPE and WHITELEY, *Thorpe's Dictionary of Applied Chemistry*, Longmans.

For a more extended treatment of specific topics, see:

- ABRAHAM, *Asphalts and Allied Substances*, Van Nostrand.
 ALEXANDER, *Glue and Gelatin*, Reinhold.
 ALLEN, *Industrial Fermentations*, Reinhold.
 BARNETT, *Coal Tar Dyes and Intermediates*, Van Nostrand.
 BROCKMAN, *Electro-Organic Chemistry*, Wiley.
 BROOKS, *The Science of Petroleum*, Oxford University Press.
 BURK and GRUMMITT, *The Chemistry of Large Molecules*, Interscience.
 BURK, WEITH, THOMPSON, and WILLIAMS, *Polymerization and Its Applications*, Reinhold.

- CAIN, *Manufacture of Dyes*, Macmillan.
- CROSS and BEVAN, *Cellulose*, Longmans.
- D'ALELIO, *Laboratory Manual of Plastics and Synthetic Resins*, Wiley.
- DAVIS and BLAKE, *Chemistry and Technology of Rubber*, Reinhold.
- EGLOFF, *Reactions of Pure Hydrocarbons*, Reinhold.
- ELLIS, *Chemistry of Petroleum Derivatives*, Reinhold.
- ELLIS, *Chemistry of Synthetic Resins*, Reinhold.
- FINNEMORE, *The Chemistry of Essential Oils*, Benn.
- GILDEMEISTER and HOFFMAN, *The Volatile Oils*, Wiley.
- GREEN, *Systematic Survey of the Organic Coloring Matters*, Macmillan.
- GRUSE and STEVENS, *Chemical Technology of Petroleum*, McGraw-Hill.
- HAWLEY and WISE, *The Chemistry of Wood*, Reinhold.
- HENRY, *The Plant Alkaloids*, Blakiston.
- HEUSER, *The Chemistry of Cellulose*, Wiley.
- HILDITCH, *Chemical Constitution of Natural Fats*, Wiley.
- IPATIEFF, *Catalytic Reactions at High Temperatures and Pressures*, Macmillan.
- JACOBS, *War Gases*, Interscience.
- JAMIESON, *Vegetable Fats and Oils*, Reinhold.
- LANDOLT, *The Optical Rotating Power of Organic Substances and Its Practical Applications*, Reinhold.
- LAWRIE, *Glycerol and Glycols*, Reinhold.
- LUCAS, *Forensic Chemistry*, Longmans.
- MAREK and HAHN, *Catalytic Oxidation of Organic Compounds in the Vapor Phase*, Reinhold.
- MARSHALL, *Explosives*, Blakiston.
- MAYER and COOK, *Chemistry of Natural Coloring Matters*, Reinhold.
- MELLAN, *Industrial Solvents*, Reinhold.
- MERCK, *Chemical Reagents*, Van Nostrand.
- MEYER, *Natural and Synthetic High Polymers*, Interscience.
- MORGAN, *Organic Compounds of Arsenic and Antimony*, Longmans.
- OTT, *Cellulose and Cellulose Derivatives*, Interscience.
- PARRY, *Chemistry of Essential Oils and Artificial Perfumes*, Scott, Greenwood, London.
- PERKIN and EVEREST, *Natural Organic Coloring Matters*, Longmans.
- POUCHER, *Perfumes and Cosmetics*, Van Nostrand.
- POWERS, *Synthetic Resins and Rubbers*, Wiley.
- PRENTISS, *Chemicals in War*, McGraw-Hill.
- RAIZISS and GAVRON, *Organic Arsenic Compounds*, Reinhold.
- SABATIER and REID, *Catalysis in Organic Chemistry*, Van Nostrand.
- SHREVE, *Dyes Classified by Intermediates*, Reinhold.
- SIMONDS, *Industrial Plastics*, Pitman.
- SIMONS and ELLIS, *Handbook of Plastics*, Van Nostrand.
- SUTER, *Organic Chemistry of Sulfur*, Wiley.
- WALTON, *A Comprehensive Survey of Starch Chemistry*, Reinhold.
- WEST and GILMAN, *Organomagnesium Compounds in Synthetic Chemistry*, National Research Council.
- WHITMORE, *Organic Compounds of Mercury*, Reinhold.
- WILSON, *Chemistry of Leather Manufacture*, Reinhold.
- WORDEN, *Technology of Cellulose Esters*, Reinhold.
- WREN, *The Organo-Metallic Compounds of Zinc and Magnesium*, Van Nostrand.

HISTORY OF CHEMISTRY

The proper background for the study of chemistry can often be obtained from the history of the science. It helps to put in their proper perspective the various branches of chemistry and of its applications. Among the histories of chemistry written in English or translated into it, we may mention the following:

- DAMPIER, *A History of Science*, Macmillan.
FINDLAY, *Hundred Years of Chemistry*, Macmillan.
HALE, *American Chemistry*, Van Nostrand.
LOWRY, *Historical Introduction to Chemistry*, Macmillan.
MASSON, *Three Centuries of Chemistry*, Benn.
MEYER, *History of Chemistry*, Macmillan.
MOORE, *History of Chemistry*, McGraw-Hill.
PARTINGTON, *Origins and Development of Applied Chemistry*, Longmans.
PHILIP, *Achievements of Chemical Science*, Macmillan.
SMITH, *Chemistry in America*, Appleton-Century.
THORPE, *Essays in Historical Chemistry*, Macmillan.
THORPE, *History of Chemistry*, Putnam.

The biographies of chemists often supply a good deal of information about their work. In this connection these few titles should be of interest:

- Chemical Society Memorial Lectures*, Gurney and Jackson, London.
HARROW, *Eminent Chemists of Our Time*, Van Nostrand.
TILDEN, *Famous Chemists*, Dutton.
VALLERY-RADOT, *The Life of Pasteur*, Doubleday.

Memorial notices and lectures appear in current chemical journals, particularly the *Journal of the American Chemical Society* and the *Journal of the Chemical Society* (London).

REFERENCE BOOKS FOR ORGANIC CHEMISTRY

There are several reference works which organic chemists use constantly and which even beginners should know about. The standard, indispensable reference is "Beilstein," *Handbuch der organischen Chemie* (Springer, Berlin), which was started around the turn of the century by Beilstein. The fourth edition, now current (1944) in 29 volumes (covering the literature through 1909), also includes a first series (27 vol., through 1919) as well as a second series (in process, through 1929) of supplementary volumes.

HUNTRESS, *A Brief Introduction to the Use of Beilstein's Handbuch der organischen Chemie* (Wiley), provides a concise outline of the classification scheme used in the fourth edition of Beilstein.

There are two formula indexes of organic compounds which can be used in conjunction with Beilstein. They are:

RICHTER, *Lexikon der Kohlenstoffverbindungen*, Voss, Hamburg; through 1909.

STELZNER, *Literatur Register der organischen Chemie*, Vieweg, Braunschweig; covers 1910-1921.

For information beyond 1921, journals should be used, particularly the abstract journals, which cover the literature thoroughly.

Smaller useful references whose contents are indicated in most cases by their titles are listed also.

HEILBRON, *Dictionary of Organic Compounds*, Oxford University Press.

HODGMAN, *Handbook of Chemistry and Physics*, Chemical Rubber Publishing Co.; reissued yearly, contains all kinds of data.

International Critical Tables, McGraw-Hill.

LONG, *Handbook of Chemistry*, Handbook Publishers; reissued frequently.

PERRY, *Chemical Engineers' Handbook*, McGraw-Hill.

SCUDDER, *The Electrical Conductivity and Ionization Constants of Organic Compounds*, Van Nostrand.

SEIDELL, *Solubilities of Inorganic and Organic Substances*, Van Nostrand.

TURNER, *Condensed Chemical Dictionary*, Reinhold.

WATTS, *Dictionary of Chemistry*, Longmans.

WINTHER, *Zusammenstellung der Patente auf dem Gebiete der organischen Chemie*, Topelmann, Giessen.

LITERATURE OF CHEMISTRY

Of course, only first-hand acquaintance will really give information about a book's contents. Short of that, several good guides to chemical literature supply competent descriptions and advice. We can recommend:

CRANE and PATTERSON, *A Guide to the Literature of Chemistry*, Wiley.

MELLON, *Chemical Publications*, McGraw-Hill.

SOULE, *Library Guide for the Chemist*, McGraw-Hill.

The primary, most direct, and most recent sources of chemical information are the journals, of which we shall name only some of the outstanding American ones:

Annual Reviews of Biochemistry.

Chemical Abstracts.

Chemical and Metallurgical Engineering.

Chemical Reviews.

Industrial and Engineering Chemistry.

Journal of the American Chemical Society.

Journal of Biological Chemistry.

Journal of Chemical Education.

Journal of Organic Chemistry.

Journal of Physical Chemistry.

Transactions of the Electrochemical Society.

For those who will progress sufficiently to refer to advanced works and journals, a fair knowledge of German and a few other foreign languages (French, Russian, etc.) will be an asset. Several dictionaries have been prepared specifically for scientific work. The *German-English* and *French-English Dictionaries for Chemists*, Wiley, by PATTERSON, are especially useful. CALLAHAM, *Russian-English Technical and Chemical Dictionary*, Wiley, and NEWMARK, *Dictionary of Science and Technology in English-French-German-Spanish*, Philosophical Library, may be of use also.

LATIN AND GREEK ROOTS IN CHEMICAL TERMINOLOGY ¹

To increase the legibility and simplify the typographic work, Greek characters have been transliterated. The letters L and G indicate Latin and Greek origin, respectively.

Root	Source		Meaning	Examples
a-	a-	G	without	amorphous
acet-	acetum	L	vinegar	acetic
acicul-	acicula	L	little needle	acicular
acroö-	a-chromos	G	colorless	acroödextrin
actin-	aktis	G	ray	actinium
adip-	adeps	L	fat	adipic, adipose
adsorp-	adsorbeo	L	draw towards	adsorption
aetio-	aitia	G	cause	aetioporphyrin
alb-	albus	L	white	albumen
allia-	allium	L	garlic	alliaceous
allo-	allos	G	different, other	allotropic
alumin-	alumen	L	alum	aluminum
ampho-	ampho	G	different, other	amphoteric
amygdal-	amydala	L	an almond	amygdalin
amyl-	amylum	L	starch	amylodextrin
an-	ana	G	up	anode
antho-	anthos	G	flower	anthocyan
anti-	anti	G	opposite, against	syn- and anti- forms
aqua	aqua	L	water	aqueous
argent-	argentum	L	silver	argenticyanide
argon	argon	G	inactive	argon
aster-	aster	G	star	asterism
atom-	atomos	G	undivided	atomic
auro-	aurum	L	gold	aurous, aurin
auto-	autos	G	self	auto-oxidation
auxo-	augeo	L	to increase	auxochrome
bar-	barus	G	heavy	barium, barometer
batho-	bathos	G	deep	bathochrome
bi-	bis	L	twice	bisulfate
bio-	bios	G	life	biochemistry
brevium	brevis	L	short	brevium
brom-	bromos	G	stench	bromine
cacodyl-	kakodes	G	ill-smelling	cacodylic
cadav-	cadaver	L	corpse	cadaverine
caes-	caesius	L	sky-blue	caesium
caesium	caesius	L	bluish-gray	caesium
calcium	calx	L	lime	calcium- calcite
calor-	calor	L	heat	calorie, calorimeter
capill-	capillus	L	hair	capillary
capr-	caper	L	goat	capric, caproic
carbo-	carbo	L	coal	carbon, carbide
case-	caseus	L	cheese	casein
cata- }	kata	G	down	cathode, cation
cath- }				
celest-	celestis	L	heavenly	celestite

¹ Reprinted by permission from G. R. Beezer's article in *Journal of Chemical Education*, Vol. 17, p. 63 (February, 1940).

Root	Source		Meaning	Examples
centi-	centum	L	hundred	centimeter
cephal-	cephale	G	head	cephalin
cerebro-	cerebrum	L	brain	cerebrosides
cet-	cete	L	whale	cetyl
chalco-	chalkos	G	brass	chalcopyrite
chlor-	chloros	G	greenish yellow	chlorine, chlorophyll
chol-	chole	G	bile	cholic, cholesterol
-chore	chore	G	volume	isochore, parachor
chrom-	chromos	G	color	dichromic, chromium
chryso-	chrysos	G	golden yellow	chrysoberyl
citr-	citrus	L	citron tree	citric
-clast	klastein	G	to break	proteoclastic
-clinic	clino	G	to lean	triclinic
coagulat-	coactum	L	driven together	coagulation
colloid-	kolla	G	glue	colloidal
conchoid-	concha	L	shell-like	conchoidal
cono-	conos	G	cone	conoscope
cosmo-	kosmos	G	world	microcosmic
creat-	kreas	G	meat	creatine
croceo-	croceus	L	saffron-yellow	croceo-salt
cruor-	cruor	L	blood	cruorin
cryo-	cryos	G	cold, frost	cryoscopic
crypto-	kryptos	G	hidden	cryptocrystalline
cupr-	cuprum	L	copper	cupric, copper
cyan-	cyanos	G	deep blue	cyanide, hemocyanin
cyclo-	kuklos	G	circle	heterocyclic
cyto-	cytos	G	cell, hollow	cytochrome
deca-	deka	G	ten	decahydrate
decrepit-	de-crepare	L	to creak, rattle	decrepitation
deliques-	liquescere	L	to become fluid, melt	deliquescent
dendr-	dendron	G	tree	dendritic
des-	de-	L	indicates privation	désoxybenzoin
desmo-	desmos	G	a bond	desmotropism
deuter-	deuteros	G	second	deuterium
dextro-	dexter	L	right	dextrose
di-	dis	G	twice	dichromate
diabatic	diabaino	G	to go through	adiabatic
ditrigon-	di-trigonos	G	twice three-cornered	ditrigonal
dodec-	dodeka	G	twelve	dodecane
dulci-	dulcis	L	sweet	dulcitol
dynam-	dynamis	G	power, force	thermodynamics
dyspros-	dysprositos	G	hard to get at	dysprosium
efflores-	efflorescere	L	to blossom, bloom	efflorescent
emanat-	emanare	L	to flow out	emanation
en-, endo-	en, endo	G	within, inside	endothermic
enantio-	enantios	G	opposite	enantiomorphic
enzym-	en-zyme	G	in yeast	enzymic
eos-	eos	G	dawn	eosin
-eresis	aireo	G	to draw	syneresis
erythro-	erythros	G	red	erythrodextrin
eu-	eu	G	well, easily	eutectic
exfoliat-	ex, folium	L	out, leaf	exfoliation
exo-	ex	G	outside, out of	exothermic
fer-	fero	L, G	to carry	argentiferous
ferro-	ferrum	L	iron	ferrocyanide

Root	Source		Meaning	Examples
fili-	filum	L	thread	filiform
flavo-	flavus	L	yellow	flavo-salt
flocc-	floccus	L	flock of wool	flocculent
fluor-	fluere	L	to flow	fluorescence, fluorine
furfur-	furfur	L	bran	furfural
Galli-	Gallia	L	France	Gallium
gen-	genao	G	to produce, make	ionogen, hydrogen
glu(y)co-	glukos	G	sweet	glucose, glycogen
halo-	hals	G	salt	halogen, halide
helio-	helios	G	the sun	helium
hemi-	hemi	G	a half	hemihydrate
hemo-	haima	G	blood	hemocyanin
hepta-	hepta	G	seven	heptane, heptose
hetero-	heteros	G	other, different	heterocyclic
hexa-	hex	G	six	hexahydrobenzene
hippo-	hippos	G	horse	hippuric
histo-	histion	G	tissue	histidine
homo-	homos	G	same	homologous
horde-	hordeum	L	barley	hordein
hydro-	hudor	G	water	hydrate, hydrogen
hygro-	hygros	G	wet, moist	hygroscopic
hypo-	hypo	G	under, lower than	hypochlorous
indium	Indium	L	indigo-blue	Indium
infra-	infra	L	beneath	infra-red
intumesc-	intumescere	L	swell up	intumescence
iodo-	iodes	G	violet-like	iodine
irid-	iris	G	rainbow	iridium, iridescent
iso-	isos	G	similar	isotope, isomorphic
kinet-	kinesis	G	a moving	kinetic
krypton-	kryptos	G	hidden	krypton
kyn-	kynos	G	dog	kynurenic
lac-	lac	L	milk	lactose, lactic
lamell-	lamina	L	plate	lamellar
lanthan-	lanthanein	G	to be concealed	lanthanum
leuco-	leukos	G	white	leuco-base
levo-	laevus	L	left	levulose, <i>l</i> -form
lign-	lignum	L	wood	lignocellulose
lipo-	lipos	G	fat	lipoid, lipolytic
lithium	lithos	G	stone	lithium
lumin	lumen	L	light	luminescence
lutecium	lutetia	L	Paris	lutecium
-lytic }	luo	G	decompose	hydrolytic, -lysis
-lysis }				
macro-	makros	G	large	macroanalysis
mal-	malum	L	apple	malic
malle-	malleus	L	hammer	malleable
melan-	melas	G	black	melanin
mell-	mel	L	honey	mellitic
-mer	meros	G	a part	isomer, tautomer
meso-	mesos	G	middle	mesoxalic
metabol-	metabole	G	alter	metabolic
micro-	mikros	G	small	microanalysis
mimet-	mimesis	G	imitation	mimetic
molecule	molecula	L	a small body	molecule
mono-	monos	G	one, single	monobasic

Root	Source		Meaning	Examples
mord-	mordeo	L	bite, eat into	mordant
morph-	morphe	G	form	isomorphic
muta-	muto	L	change	mutarotation
neon-	neos	G	new	neon
nephelo-	nephele	G	a cloud	nephelometry
nitro-	nitrum	L	native soda	nitrogen
nona-	nonus	L	ninth	nonane
octa-	octo	L, G	eight	octane
-ode	hodos	G	road	anode, cathode
ole-	oleum	L	oil	oleic
osmium	osme	G	smell	osmium
oxy-	oxus	G	bitter, acidic	oxygen
pect-	pektos	G	congealed	pectin
pent-	pente	G	five	pentoxide
peps-	pepsis	G	digestion	peptize, pepsin
per-	per-	L	excess, more	perchloric
petr-	petra	L	rock	petroleum
phanero-	phanein	G	to be visible	phanerocrystalline
-phile	phileo	G	to love	lyophilic
phlogiston	phlogisteo	G	to set on fire	phlogiston
-phobe	phobia	G	fear	lyophobic
phor-	fero	L, G	to carry	cataphoresis
phos- }	phos	G	light	photosynthesis
photo- }				
-phyll	phyllon	G	leaf	chlorophyll
phyto-	phyton	G	plant	phytosterols
picric	pikros	G	bitter-	picric
piezo-	peizein	G	to exert pressure	piezochemistry
pinaco-	pinako-	G	mirror image	pinacol
piper-	piper	L	pepper	piperazine
pleo-	pleio-	G	many, more	pleochroism
plumb-	plumbum	L	a leaden ball	plumbite
porphyr-	porphyra	G	purple	hematoporphyrin
potential	potentia	L	power	potential
praeseo-	prasios	G	leek-green	{ praseodymium
proteo-	proteos	G	original	{ praeseo-salt
pseudo-	pseudos	G	false	proteolytic
pulver-	pulvis	L	dust	pseudo-alums
pycno-	puknos	G	dense	pulverulent
pyro-	pur	G	fire	pycnometer
quantum	quantum	L	how much	pyrophosphate
quatern-	quater	L	four times	quantum mechanics
racem-	racemus	L	cluster	quaternary
ren-	renes	L	kidneys	racemic
retic-	rete	L	net	adrenalin
rhodium	rhodon	G	a rose	reticulated
rub-	ruber	L	red	rhodium
salic-	salix	L	willow	bilirubin, rubidium
sarco-	sarkos	G	of flesh	salicylic
sclero-	skleros	G	hard	sarcosine
selen-	selene	G	moon	scleroprotein
semi-	semi-	L	half	selenium, selenide
sesqui-	sesqui-	L	one and a half	semihydrate
silic-	silex	L	a flint	sesquioxide
				silicon, silicate

Root	Source		Meaning	Examples
solut-	solutum	L	dissolved	solution
solv-	solvens	L	dissolving	solvent
sphenoid-	sphen	G	a wedge	sphenoidal
stalact-	stalaktos	G	oozing in drop	stalactite
stann-	stannum	L	tin	stannic
stereo-	stereos	G	volume, space	stereochemistry
stero-	stear	G	tallow	stearic
stib-	stibium	L	antimony	stibine
striat-	stria	L	furrow	striated
succin-	succinum	L	amber	succinic
sucr-	sucrum	L	sugar	sucrose
super	super	L	above	superphosphate
syn-	syn	G	with, on same side	syn- and anti- form
synthet-	syn, titheimi	G	to put together	synthetic
tauto-	tautos	G	same	tautomeric
tect-	teko	G	melt	eutectic
tellur-	tellus	L	earth	tellurium
ter-	ter	L	three times	terchloride
tetra-	tessares	G	four	tetroxide
thallium	thallos	G	green twig	thallium
thalp-	thalpos	G	heat, warmth	enthalpy
thermo-	thermos	G	heat	thermoluminescence
thio-	theios	G	sulfur	thiosulfate
thixo-	thixis	G	touch	thixotropic
topo-	topos	G	place, arrangement	isotope
tri-	tres	L	three	trimethylamine
tribo-	tribo	G	rub	triboluminescence
trop-	trepo	G	turn, change	allotropic
trunc-	truncatus	L	cut off	truncated
ultra	ultra	L	beyond	ultraviolet
undec-	undecim	L	eleven	undecane
uni-	unus	L	one	univalent
vitr-	vitrum	L	glass	vitreous
xantho-	xanthos	G	yellow	xanthoproteic
xenon	xenos	G	stranger	xenon

Prefixes employed by the chemist to designate the numbers of atoms or radicals in a molecule, the number of molecules of water of crystallization, and so forth, are all taken literally from the Latin or Greek. It would well pay any student of chemistry, to commit to memory the lower numerals:

	Latin	Greek
1	unus	eis
2	duo	duo
3	tres	tres
4	quattuor	tessares
5	quinque	pente
6	sex	hex
7	septem	hepta
8	octo	okto
9	novem	ennea
10	decem	deka

Letters of the Greek alphabet are employed by chemists, physicists, and mathematicians.

Alpha	α	A	Nu	ν	N
Beta	β	B	Xi	ξ	Ξ
Gamma	γ	Γ	Omicron	\omicron	O
Delta	δ	Δ	Pi	π	Π
Epsilon	ϵ	E	Rho	ρ	P
Zeta	ζ	Z	Sigma	σ	Σ
Eta	η	H	Tau	τ	T
Theta	θ	Θ	Upsilon	υ	Υ
Iota	ι	I	Phi	φ	Φ
Kappa	κ	K	Chi	χ	X
Lambda	λ	Λ	Psi	ψ	Ψ
Mu	μ	M	Omega	ω	Ω

The use of the terms *ortho*, *meta*, and *para* to designate the positions of elements or groups in disubstituted benzene is purely conventional, as *ortho* and *para* both signify *alongside of*. More exactly, an interchange of the two terms would better preserve their original meaning, for primarily *para* means *alongside of* and *ortho*, *straight*. *Meta* signifies *in the midst of* or *between*, and is hence properly used to designate the position between *ortho* and *para*.

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